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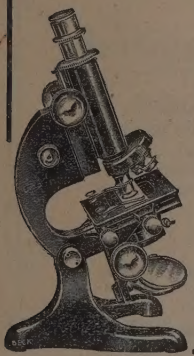

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 40.] 1943. [No. 3.

SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

Epidemiology.

DRENSKY (p. 602) states that in Bulgaria the chief malarial regions are found along the great rivers (Danube, Maritza and Struma) and in the coastal region. In the Danube region *Plasmodium vivax* only is found ; on the coast and in the Struma region *P. falciparum* becomes more common than *P. vivax* in autumn, and spleen rates reach 80–100 per cent. Mortality is highest in the Struma area.

The Department of Health of Palestine (p. 592) describes the great reduction in malaria which has been effected since 1918. The Jordan valley is still heavily infected, but many of the areas previously dangerous have been controlled with success. *P. vivax* is most in evidence from June to September, *P. falciparum* from August to December ; *P. malariae* is rare.

VISWANATHAN (p. 251) states that the transmission season in tea estates in Upper Assam, where *Anopheles minimus* is the vector, is from May to January inclusive, *P. vivax* infections are most prevalent from May to July ; *P. falciparum* infections are commoner throughout than *P. vivax*, but are especially seen in the last quarter of the year.

As is well known, malaria in Ceylon, in normal years, is most prevalent in the dry zone of the north and east, and is least common in the wet zone of the south-west. The intermediate zone is subject to great fluctuations in spleen rates. SIVALINGHAM and RUSTOMJEE (p. 663) confirm these findings and give an account of a very extensive series of examinations carried out in children. Spleen rates varied from 40–60 per cent. in the dry zone to 0·10 per cent. in the wet zone. In the dry and intermediate zones *P. malariae* was the commonest parasite, *P. falciparum* next, and *P. vivax* least ; in the wet zone the three were more evenly distributed.

TANAKA (p. 251) states that benign tertian and subtertian malaria are endemic in the Yulin district of Hainan. He gives a list of the Anopheles found, but no indication of the principal vectors.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1942, Vol. 39. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

Faust (p. 388) notes that in the United States all the naturally acquired malaria is due to *P. vivax* except in the South, where *P. falciparum* is found. He discusses the distribution of malaria in the Southern States.

Carr *et al.* (p. 513) have carried further their investigations of malaria in Cuba. *P. vivax* was much more common than *P. falciparum*; *P. malariae* was not found. The association of low parasite rates with higher spleen rates is an indication that malaria has not recently been active, and it is recorded that the last epidemic in the Camaguey Province, under investigation, occurred in 1934. The practice of importing labour for the cane harvest has been abandoned in recent years, and it is thought that this has probably reduced the incidence of epidemic malaria. Carr and Meléndez (p. 514) give a similar report on the Province of Pinar del Rio, Cuba, noting that malaria is most common along the coastal plain below a height of 100 feet. Carr *et al.* (p. 515) have found very little endemic malaria in the Havana Province of Cuba, and attribute this to the porous nature of the soil. Breeding of *A. albimanus* takes place, however, on the comparatively impervious soil of the valley of the Almendares river, where rain and irrigation water tends to collect, and where borrow pits afford opportunity for stagnation of water in the rainy season.

Ram (p. 736) gives an account of malaria in British Honduras, where *P. falciparum* infections are more common than *P. vivax*; *P. malariae* is found occasionally.

Kumm and Ruiz (p. 290) have conducted a malaria survey of Costa Rica, where the disease is most prevalent in the low-lying provinces. *P. vivax*, *P. falciparum* and *P. malariae* are found, the latter especially along the Pacific coast. Spleen rates in children are given, and are related to the parasites found. The evidence gained indicates that *A. albimanus* is by far the most important, if not the only, vector, but a list is given of the other anophelines found.

Lobo (p. 292) states that although in Europe rice cultivation may lead to the breeding of non-vector races of *A. maculipennis*, and may, therefore, not necessarily lead to malaria, the position in the rice-fields of Argentina is quite different. There rice cultivation invariably leads to the breeding of large numbers of *A. pseudopunctipennis*, the most important vector of the Tucumán Province, and malaria is greatly increased in the neighbourhood of the rice-fields. To control this malaria he advocates the exclusion of rice cultivation near villages, intermittent irrigation, the use of Paris green and prophylactic drugs, and the proofing of dwellings.

Noé and Neghme (p. 427) give an account of malaria in a district in the north of Chile, where *P. falciparum* and *P. vivax* infections occur, and where *A. pseudopunctipennis* is the vector.

Aetiology.

Soares (p. 293) believes that the parasite found in pernicious malaria at São Bento, Brazil, which is markedly neurotropic, can be distinguished morphologically and clinically from *P. falciparum*, and adheres to the opinion of Ziemann that *P. perniciosum* is a valid species. It is said to be very resistant to the usual anti-malaria drugs. Ferrari (p. 293) refers to the findings of Soares and supports his contention.

Archetti (p. 17) reports infections with *P. malariae* in southern Abyssinia. No *P. vivax* infections were found, but *P. falciparum* was apparently present.

Garcia (p. 116) describes what is probably *P. ovale* in a patient in the Philippines. This finding recalls Craig's original description of a similar form in 1900, in an American soldier who returned from service in those islands. Yao and Wu (p. 388) describe a parasite which was probably *P. ovale* in a patient at Kunming, China. de Zulueta (p. 809) describes *P. ovale*, found in Colombia for the first time.

Raffaele (p. 263) claims that exoerythrocytic schizonts cannot originate from merozoites formed, within red cells, from pigmented schizonts, but that they are formed from sporozoites or from merozoites of non-pigmented forms within endothelial cells. [But see Coulston and Manwell (p. 440).] In his view the fact that exoerythrocytic schizonts may follow infection induced by the inoculation of blood containing pigmented forms is due to the existence of undetected exoerythrocytic forms found in the blood inoculated. He describes and illustrates exoerythrocytic schizonts found in human malaria, one from the bone marrow in *P. falciparum* infection and two from the bone marrow in *P. malariae* infection; this is the first record of these forms in quartan malaria. Brug (p. 263) claims to have found exoerythrocytic schizonts in smears of the lung from a paralytic who died and who had been treated by induction of malaria. In comment, however, Wenyon does not accept the finding without question.

Transmission.

Russell and Rao (p. 427) have shown that in water in which the surface tension has been reduced from the normal 70 to 27–36 dynes per cm., anopheline larvae cannot attach themselves to the surface, and that they sink and drown. There was no significant difference between species, and no correlation could be found between the surface tension of natural waters and the presence or absence of larvae, but in natural waters no surface tension below 65·5 dynes was found.

It seems, from an experiment carried out by Boyd *et al.* (p. 431) that anophelines feeding on a person infected with two strains of *P. vivax* may become infected with one strain only, or with both, and in that case may be able simultaneously to propagate both strains.

Toumanoff (p. 117) discusses the composition and formation of the "black spores" found in some infected mosquitoes.

Bates (p. 389) reports on field observations of Anopheles in Albania. Here intense malaria is associated with *A. maculipennis* var. *sacharovi* which breeds typically in marshes, and also in pools and ditches and in water containing 2 per cent. or more of sodium chloride. He discusses the factors which limit the geographical distribution of this and other varieties, among which are probably the extremes of summer and winter temperatures, and the variations in atmospheric humidity, which affect the adults. There is reason to think that some malaria may be carried by one or more of the varieties *typicus*, *messeae* and *subalpinus*, which are usually considered to be innocuous because they do not readily attack man. In the areas in which *sacharovi* is not found, the principal vector is *A. superpictus*, which breeds typically in the small pools of gravel river beds, but which, late in the season, when the adult population has reached its maximum, may breed in other pools and in rice fields. The other Anopheles found

include *A. hyrcanus*, *A. algeriensis*, *A. plumbeus* (breeding in tree holes only), *A. claviger* and *A. marteri*. DRENSKY (p. 602) states that in the Danube region of Bulgaria the common anophelines are *A. maculipennis messeae* and *typicus*; malaria is present but not intense. In the coastal area and the Struma region *A. maculipennis sacharovi* (*elutus*) and *typicus*, and *A. superpictus* are found; malaria is there much more intense. KOMÁREK and BREINDL (p. 595) found *A. maculipennis typicus* and *messeae*, and *A. bifurcatus* (*claviger*) in Moravia and Bohemia, and describe their habits.

WEYER and HUNDERTMARK (p. 428) have found experimentally that there is no significant difference between the temperatures of water preferred for oviposition by *A. maculipennis* (*typicus*, *messeae*, *atroparvus* and *labranchiae*) and *A. superpictus*. The experiment, therefore, offers no explanation of geographical distribution of these mosquitoes, but it shows that water temperature is not the only important factor in the choice of breeding place.

KHODUKIN and SHTERNGOL'D (p. 116) record results obtained in their investigations in Tashkent on the cold-resistance of *A. superpictus*, *A. pulcherrimus* and *A. maculipennis sacharovi*. In Tashkent *A. superpictus* and *A. sacharovi* usually hibernate in buildings in which the temperature does not fall below −7°C.; there is probably, therefore, no great mortality of the adults in winter. Information is given of the hatching of eggs kept for 16 hours at −4°C. RAEVSKII (p. 253) has made studies on the microclimate of the winter quarters of hibernating *A. maculipennis* var. *messeae*; the details must be sought in the original abstract.

The Department of Health of Palestine (p. 592) have issued a review of malaria in the period 1918–1941. The common vectors are described (*A. bifurcatus*, *A. sacharovi* (*elutus*), *A. sergenti*, *A. superpictus*, *A. hyrcanus* var. *sinensis* and *A. algeriensis*) and an account of their breeding places is given.

HADDOW (p. 595) has shown, by controlled work in huts in Kenya, that *A. gambiae* and *A. funestus* are true house-haunting species, entering houses principally shortly before dawn, preferring houses with numerous human inhabitants, especially if unwashed, attracted to a hut containing dirty clothing, attracted but little to a calf. In this area the incidence of *A. gambiae* depends on the local rainfall; that of *A. funestus* increases with rise in the level of Lake Victoria, and depends therefore not on local but on general rainfall of a large part of East Africa.

BRAMBILLA (p. 391) gives a list of the anophelines found near Dirre Daua, Abyssinia; the commonest was *A. gambiae*. ARCHETTI (p. 17) has found *A. gambiae* and *A. pharoensis* in southern Abyssinia.

DE MEILLON and PEREIRA (p. 294) discuss the identification of anophelines of the *funestus* group in Portuguese East Africa.

HOPKINS (p. 391) shows that on the northern shore of Lake Victoria *A. funestus* is capable of travelling two miles down wind from its breeding place, and that under these circumstances it caused extensive malaria in an institution.

BLACKLOCK and WILSON (p. 253) have shown that in Freetown, Sierra Leone, engorged *A. gambiae* tend to rest in shrubs during the daytime. In Java VENHUIS (p. 254) has made the somewhat similar observation that whereas of female *A. maculatus* caught in houses only about one-third contained blood, of those caught on the steep, shadowy and moist banks of the streams, practically all were engorged.

VENHUIS (p. 736) notes also that other anophelines, especially *A. aconitus*, are to be found resting on the steep, dark and damp banks of streams. In such localities infected *A. minimus* var. *flavirostris* have been found, whereas no infected specimens were caught in houses or stables (p. 737). He emphasizes the importance of search in these and other natural haunts.

GENEVRAY and TRY (p. 177) report on the area of moderate malaria endemicity in the Tong area of Indo-China, where, of the many potential vectors, *A. aconitus* is the most widespread.

THOMSON (p. 293) has continued his studies on the behaviour of *A. minimus*. He notes that in waters favoured by this mosquito, the amount of organic matter and the degree of pollution are consistently lower than elsewhere; yet gravid females do not appear to be able to distinguish water from the normal breeding place and water not ordinarily used, and larvae will develop in both. This subject requires further investigation. On the other hand, when water is polluted by decaying vegetation, even in very high dilutions, gravid *A. minimus* are repelled; clearly the sensitivity of the female is the essential factor in control by herbage packing. The controlling effect usually attributed to silt in rivers is probably due, not to the silt, but to increase in stream velocity. He (p. 597) notes that *A. minimus* has, apparently, no marked reaction to differences in humidity, but has a strong tendency to avoid high temperatures. The temperature fatal to adults is several degrees lower than that fatal to *A. vagus*. Most blood meals are taken after midnight, and blood feeding takes place throughout the year; there is no hibernation in cold weather.

The same author (p. 597) has shown that in suitable places there is a considerable output of female *A. minimus* in January, the coldest month of the year. The breeding places at this time are in perennial rivers or seepages and small streams; these must be included in any control scheme, and the most convenient method probably consists of the removal of grassy edges and the exposure of the bare banks to sunlight. In the period February to April there is a great increase in larval density and output of adults.

VISWANATHAN (p. 428) gives the results of a 10-year investigation in Assam, where *A. minimus* is the principal vector throughout; in this mosquito sporozoites were found every month except February. The other vectors are not of much importance except in localized areas: *A. annularis* was found to be infected in one district only, *A. culicifacies* similarly in one area only, *A. maculatus* was infected in Shillong, but the malaria prevalence was low there in 1940 when the influence of *A. minimus* was slight; in Shillong *A. maculatus* is markedly zoophilic. A very few specimens of *A. philippinensis* and *A. aconitus* were infected; they are of little importance. Similar findings for the year 1940–41 are given by VISWANATHAN *et al.* (p. 598).

CLARK and CHOUDHURY (p. 177) show that in Assam, *A. leucosphyrus* is a serious vector of malaria among people who live on the edge of jungle country, and that in such people the malaria may be intense. In these districts the mosquito breeds in small collections of stagnant water. In comment BUXTON points out that, although it was previously known that *A. leucosphyrus* was a carrier, it was often dismissed as a "jungle species" not normally seen if not looked for. The finding of the present authors may have an importance not yet realized for India, Burma, Malaya, the Dutch East Indies and the Philippines.

Russell and Rao (p. 598) have studied the seasonal prevalence of 12 species of Anopheles in S.E. Madras, paying most attention to *A. culicifacies*. This mosquito is most prevalent in August–September as a result of irrigation, which begins in June, but afterwards the density declines for reasons which are not clear. These authors (p. 599) state that the principal breeding places of *A. culicifacies* in the Tanjore District of Madras are collections of water in borrow pits, but that as the pits grow older the numbers of larvae decline. This decline is associated with the increase of blue-green algae, amorphous organic matter and total plankton, yet under these conditions the development of larvae is not adversely affected. If these conditions are the cause of the decline, therefore, their effect must be upon the egg-laying females, which choose the newer waters of fresh borrow pits for oviposition. Many other factors were investigated, but were found to have no influence.

Russell and Mohan (p. 391) have bred *A. stephensi* in tap water and from these colonies have established others which will breed in water containing as much as 80 per cent. sea water. Experiments have shown that these changes in the chemical composition of the larval environment do not modify the capacity of the emerging *A. stephensi* to transmit *P. falciparum*.

Sen (p. 810) enumerates the anophelines found in trains and boats arriving in Calcutta, noting in particular that *A. sundaicus* is found and has probably become established in salt lakes east of Calcutta as a result of boat transport. He (p. 294) has studied the relationship between 12 common aquatic plants and the same number of species of Anopheles near Calcutta. Certain species are not found in association with certain plants. The results cannot be summarized, but it appears that a practical result of such studies may be that plants may give an indication of the prevalence of certain mosquitoes.

Boyd (p. 429) has investigated the infecting power, for *A. quadrimaculatus*, of patients infected with *P. vivax*. Good infectors in general have higher gametocyte densities than poor infectors, and the sexes of the gametocytes are more equal. Yet density alone is not a reliable guide to infecting power, and susceptibility of mosquitoes in different batches possibly affects the qualitative infection of any batch, especially when gametocyte density is low. The gametocytes of good infectors are probably of greater vitality than those of the poor infectors.

Hurlbut and Hewitt (p. 295) note that *A. quadrimaculatus* may be infected with *P. lophurae*, an avian parasite, and point out that in human malaria investigations, oöcyst and sporozoite indices are used, and that confusion between infection with *P. lophurae* and the human parasites is therefore possible.

Vargas *et al.* (p. 430) have shown that in a district of Mexico *A. pseudopunctipennis* is the only important vector, and point out that in other regions of America, where this mosquito occurs with recognized carriers such as *A. albimanus* and *A. tarsimaculatus*, its importance is apt to be overlooked or uncertain. Vargas (p. 295) distinguishes four varieties of *A. pseudopunctipennis* by morphological differences in the eggs. Kumm (p. 296) has noted variations in the eggs of certain anophelines in Costa Rica, the significance of which is not clear.

Bocalandro and Wilde (p. 115) note that the most important, and probably the sole, vector in Argentina is *A. pseudopunctipennis*, although other anophelines, such as *A. argyritarsis*, are more prevalent.

Lobo (p. 292) notes that *A. pseudopunctipennis* is the important vector in the Tucuman Province of Argentina; Romaña (p. 292) states that *A. albitarsis* is believed to be a vector in the Chaco territory of the same country, and is a predominant species. Both authors give lists of other prevalent anophelines.

Carr *et al.* (p. 513) note that in the Camaguey Province of Cuba *A. albimanus* is the important vector, and that *A. crucians* and *A. vestitipennis* are found. *A. albimanus* is found especially at altitudes below 100 feet along the coastal plain (p. 514); it is not common in the porous soil of the Province of Havana, except in the valley of the Almendares river, where relatively impervious soil offers opportunity for collection of irrigation water and the formation of pools in borrow pits during the rainy season (p. 515).

Komp (p. 430) notes that *A. darlingi*, a dangerous vector, has recently been found in British Honduras, Guatemala and Spanish Honduras; it had previously not been seen north of Venezuela. Kumm and Ram (p. 296) and Ram (p. 736) note that in British Honduras *A. albimanus* is the commonest anopheline; *A. darlingi* is found in restricted areas. One naturally infected specimen of *A. vestitipennis* was found, an interesting finding in view of the fact that this mosquito is not usually regarded as a vector.

Corrêa and Ramos (p. 737) report infected *A. darlingi* and *A. oswaldoi* var. *metcalfi* in the south of the State of São Paulo. Coutinho (p. 738) also reports infected specimens of the latter in Brazil.

Rozeboom *et al.* (pp. 430, 664) give an account of their discovery that *A. bellator* is a dangerous vector of malaria in Trinidad. This mosquito breeds exclusively in collections of water at the base of bromeliads which are extensively parasitic on the shade trees of cocoa plantations; it is anthropophilic and attacks chiefly in the late afternoon and evening. In the *Engineering News-Record* (p. 664) hints are given on methods of control of the breeding of *A. bellator*.

Pathology.

Vryonis (p. 178) has studied the blood in subtertian malaria in four children. The peak of reticulocytosis was reached at the 11th day of treatment, when the erythrocytes were at their lowest point; thereafter reticulocytes decreased as erythrocytes increased. As the reticulocytes decreased, leucocytes increased, with marked eosinophilia, but lymphocytes, basophiles and large mononuclears were unaffected.

Parise and Lucrezi (p. 516) have studied material obtained by spleen puncture in patients with chronic malaria who had been treated intensively with quinine. The principal finding was of hyperactivity of the reticulo-endothelial system; no definite evidence of non-pigmented free forms of the parasites could be found.

Orlina (p. 519) makes the point that in malaria the liver is as frequently enlarged as the spleen, and gives the results of investigations of functional changes. Insufficiency is not uncommon in the acute stages, and the author notes that malarial cirrhosis is common in the Kuibyshev district from which she writes.

Oedema is often seen in patients undergoing malaria therapy. Kopp and Solomon (p. 665) regard this as a result of the reduced osmotic pressure, in patients free from renal damage or cardiac failure, caused by the marked fall in plasma albumin which regularly occurs to a critical level at which oedema may be produced. Globulin tends to rise, and the albumin-globulin ratio, therefore, is very greatly reduced.

Clinical Findings.

FIELD (pp. 17, 254) gives information on his method of rapid staining of thick blood films; the whole process occupies less than 10 seconds.

VAILLANT (p. 255) draws attention to the importance of blood examination in all febrile conditions which are encountered in malarious areas. He quotes the experience at a hospital in the Sudan, to which 50 men, diagnosed as suffering from German measles, were admitted. The condition did not clear up until a medical officer, noticing enlargement of the spleen in several cases, examined the blood of all the patients, found *P. vivax* infection in each, and gave quinine. The rash was apparently typical of German measles, but it is thought probably to have been due to prickly heat brought on by the sweating induced by the malaria paroxysms.

SCHÜFFNER (p. 431) makes the point that in malaria a thorough search of a thick drop preparation by a competent person will always give positive results if the blood has been taken during a paroxysm, but a negative finding in a fever-free interval does not exclude the disease. He considers that the frequent occurrence of a prolonged incubation period in *P. vivax* infections is probably related to a cycle of development in the reticulo-endothelial system. In his view the initial fever is due to a toxin different from that which causes the intermittent paroxysms which follow, and against this toxin a firm and lasting immunity is developed.

SOUTHWELL-SANDER and HAND (p. 393), however, report cases of malaria which illustrate the contentions that diagnosis may be justifiable even though at no time can parasites be found in the blood, and that in pernicious attacks the paucity of parasites may give no indication of the severity of the condition.

DE NEGRI (p. 520) has noted the frequency with which basophile granulation of parasite-free red cells is seen in the blood of malaria patients, both in the presence and absence of parasites in the peripheral blood. He concludes that this granulation is of considerable diagnostic significance if parasites cannot be found, and that it indicates a 70 per cent. probability of a *P. falciparum* infection.

BELTRAN (p. 812) has noted the frequency with which *P. vivax* is found in reticulocytes in therapeutic infections.

ALEXANDROV (p. 250) notes that tertian malaria [presumably benign tertian] is often encountered in the Pamir mountains, even in winter, and that Anopheles are to be found at altitudes of 2,000 metres. He points out that malarial subjects, with either active or latent infection, often develop acute paroxysms on journeying from low levels to the mountains, especially if the change to high altitude is made quickly. He discusses the various factors which may be responsible for these attacks, and gives a list of diseases with which they may be confused, emphasizing especially relapsing fever due to *Spirochaeta carteri*, which is endemic in this region.

COATNEY and YOUNG (p. 600) have made detailed studies of the paroxysms due to induced *P. vivax* infections, but these cannot further be summarized.

WILE and MUNDT (p. 433) draw attention to the dangers of therapeutic malaria, showing that 29 patients in a series of 1,000 died as a result of this treatment. They give the immediate causes of death, of which circulatory collapse was the most common, and lay down the

rule that malaria therapy should only be given to patients whose hearts are well compensated. Other contraindications are mentioned, and reference is made to symptoms which should be regarded as danger signals. CHOPRA *et al.* (p. 255) have used *P. falciparum* for therapeutic malaria in India, in a patient resistant to *P. vivax*, but they point out that this infection must be closely watched in view of possible rapid increase in the intensity of the infection. They note that *P. falciparum* infection induced by blood injection is more easily controlled than that acquired naturally, but not so easily as *P. vivax* infection.

In a discussion of cerebral malaria, WRIGHT (p. 432) states that malaria can be responsible for schizophrenic or confusional states, though the pathology of these is not known. Cerebral malaria may simulate meningitis and be simulated by several infective diseases or by trauma or alcoholism. It may lead to permanent paralysis. The author quotes his experience of 16 cases. MENDEZ and HUAMAN (p. 432) describe symptoms of a cerebellar lesion arising probably from a *P. vivax* infection.

MAILYAN (p. 516) reports two cases of acute pulmonary oedema which occurred in young persons during their first attacks of malaria and which, though severe, cleared on treatment with quinine, atebrin and plasmoquine. The evidence strongly suggests that malaria was the cause of the oedema and that the patients were in the non-immune state.

SABLIN and EGOROVA (p. 519) note that in malaria patients who are suffering from lobar pneumonia, leucocytosis frequently does not occur and that there is a retardation of resolution; this failure to react as non-malarial patients commonly do, tends to lead to complications.

ZIKEYEV (p. 517) ascribes to malaria certain trophic skin lesions which cleared up under treatment with anti-malaria drugs, and quotes a case in which skin grafting in a patient subject to malaria was unsuccessful until the malaria was treated.

BYSTRITSKI (p. 520) reports on disorders of the kidney observed in malaria; in most of the cases the condition yielded to anti-malaria treatment, but in some persistent changes were produced, with uraemic symptoms.

LOPATIN (p. 518) discusses the subject of congenital malaria, of which he records 35 cases. Most of the infants are underweight at birth, and chronic disturbances of nutrition are common. These cases are often refractory to treatment, and permanent effects such as infantilism or deficient resistance to infections may ensue. The author considers that congenital malaria may be the result of intra-uterine infection due to malarial damage to the placenta, or may be due to injury of the placenta at birth. SOEDARSONO (p. 599) gives details of two cases of malaria which he considers to have been contracted *in utero*.

From the experience of a case in a child in Florida, in which he suspected that *P. malariae* infection was transmitted by blood transfusion, MARKS (p. 252) suggests that it would be wise to exclude all donors who have had malaria or who come from malarial regions. [This point of view is obviously reasonable in malaria-free countries, but cannot, of course, be sustained in countries in which the disease is endemic.] Marks goes on to say that if it is impossible to exclude such donors, the recipient should be given atebrin as a prophylactic. A further solution of the problem probably exists, as the findings of GORDON (p. 252) show. He records a case of quartan malaria due to the transfusion of stored blood from a donor in whom *P. malariae* was

subsequently found. It was previously known that this could occur if the blood was stored for eight days or less, and Gordon suggests that transfusion malaria may be avoided by using only blood which has been stored for longer than that period. In comment, Mollison points out that blood taken from subjects who have lived in malarial districts may safely be used for obtaining serum or plasma. [It would perhaps be advisable to treat donors, before taking blood, with an anti-malarial drug, though the effect of such treatment on the storage of blood would need to be watched.]

Hoch *et al.* (p. 20) have shown, by injecting intravenously into non-malarious subjects the blood of persons infected with the McCoy strain of *P. vivax*, in amounts calculated to contain small numbers of parasites, that there is a relationship between the dose and the incubation period, but that the character of the infection, once established, is independent of the infecting dose. Small, standardized doses give more uniform results than the artificial methods generally employed, and doses of 100–250 trophozoites are sufficient to induce infection.

Mollaret (p. 21) notes that blood infected with *P. vivax*, injected intramuscularly or intravenously into non-malarious subjects, without anticoagulant, may, but very rarely, give rise to paroxysms of malaria in the recipients without any incubation period.

Priest (p. 738) describes a case, diagnosed as of meningococcal septicaemia, in which the temperature showed a quartan periodicity. Parasites were not found and there was no response to quinine.

The complement fixation test in malaria has been examined by several workers, whose results show considerable uniformity. Coggeshall (p. 118) has investigated this reaction with an antigen prepared from *P. knowlesi* in the red cells of infected *Macacus rhesus*. This antigen reacts with sera from man infected with *P. vivax* or *P. falciparum*; the complement fixing antibodies appear in the serum before the peak of *vivax* infection (or about two weeks after the onset of symptoms) and persist for five months after the disappearance of circulating parasites. Wassermann-positive sera, and sera from patients with other diseases, give negative results in the absence of malaria. The test, therefore, appears to be useful in chronic infections when parasites cannot be found. Dulaney *et al.* (p. 119) report on the complement fixation test, with a *P. knowlesi* antigen, in naturally acquired malaria. About 80 per cent. of the tests were positive when parasites were present in the blood, and these positive results were found for two months or more after the parasites had disappeared. A negative result, however, cannot be regarded as excluding malaria. Kligler and Yoeli (p. 255) have also used the complement fixation test in malaria, with the *P. knowlesi* antigen prepared by Coggeshall. The test usually becomes positive during the third week after the onset, provided that the patient has had two or more paroxysms; it tends to become negative during the fourth month after the last attack.

Burney *et al.* (p. 665) have conducted an enquiry into the serological tests of syphilis, by several different methods, in patients with malaria, whose sera, before the induction of malaria, were negative to those tests. They confirm the findings of Kitchen *et al.* that positive results are often given during or after the malarial febrile period, but find that, in general, the tests become negative about one month after the termination of fever. In serological surveys to find the incidence of syphilis, therefore, regard must be paid to false positives due to malaria. As a result of a syphilis and malaria survey in

North Carolina, FELLOWS and PERRY (p. 387) are led to the opinion that natural malaria may give rise to false positive serum reactions of syphilis for a longer period than the 66 days for which they were shown to persist by KITCHEN *et al.*

From these and other experiences it is known that serum from a patient with malaria may give a positive Wassermann reaction in the absence of syphilis. In an attempt to see if a complement fixation test, in which cultured spirochaetes were used as antigen, would remain specific for syphilis EAGLE *et al.* (p. 119) found that, so far from this being so, that test gave even more positive results than the Wassermann in non-syphilitic malaria. The test, therefore, does not permit the serological differentiation of syphilis and malaria.

As a result of a study of the protein tyrosine reaction in malaria, SWARTZWELDER and ADAMS (p. 600) come to the conclusion that it has little more than a supplemental value.

D'ALESSANDRO and SICARI (p. 256) give reasons for their belief that the Henry reaction is more than a simple physico-chemical reaction, claiming that the serum globulin of malarial subjects appears to have a particular affinity for melanin. *Charles Wilcocks.*

[*To be continued.*]

RABIES.

A REVIEW OF RECENT ARTICLES. XXXVIII.*

i. *Virus.*

It has been customary to attribute the attenuation of rabies virus during the preparation of vaccine by the Pasteur method to desiccation. It has also been admitted that with the passing of the years and of the "fixed" virus (Paris) from rabbit to rabbit by intracerebral inoculation it has become more sensitive to desiccation (disappearance of virulence of the spinal cord after three to four days instead of the original six to seven days). It is true that the virus in the cord dried in air over caustic potash becomes attenuated, but it is incorrect to state that it is desiccation which is the factor. It is probably the autolysis of the tissue, the action of the "cellular proteolytic ferments" whose action is favoured by the presence of the moisture and the conditions obtaining in the slow drying technique, which accounts for the inactivation of the virus. VANSTEENBERGHE (1903) showed that if the virus of rabies is dried rapidly, for example in a thin layer on a slide *in vacuo* over sulphuric acid, it will retain its infectivity for several months. This has been amply confirmed by REMLINGER and BAILLY[1] in numerous experiments. "Street" and "fixed" virus behave similarly as regards resistance to desiccation. On the other

*For the thirty-seventh of this series see this *Bulletin*, Vol. 39, p. 589.

References marked with a † denote that the paper referred to was abstracted by Col. A. G. MCKENDRICK, who was prevented by indisposition from completing the review. The remainder of the article is the work of Dr. I. A. GALLOWAY.

[1]REMLINGER (P.) & BAILLY (J.). La dessiccation n'atténue pas le virus rabique, elle le conserve. (Premier mémoire).—*Ann. Inst. Pasteur.* 1940. Sept. Vol. 65. No. 3. pp. 130–145.

hand the virus of Aujeszky's disease is much more resistant to the slow process of desiccation over caustic potash than rabies virus. The present observations amplify those reported previously and bring them into line with what is known about the effect of desiccation on other viruses. No quantitative estimate of the degree of resistance of rabies virus to "slow" as opposed to "rapid" drying has been attempted. [The attenuation of the virus in the Pasteur method may lead to some denaturing of the virus protein. There are now known to be more perfect methods of drying virus than those previously employed. If Pasteur had employed these he would probably not have developed his method of vaccination against rabies.] As would be expected and has been proved also with other viruses, rabies virus dried "rapidly" will subsequently resist higher temperatures (105°C. and even 110°C., for two to five minutes) than virus suspended in fluid.

As Remlinger and Bailly[2] point out, reference has been made frequently in the literature to the existence of so-called "reinforced strains" of rabies virus. There are few countries in which they have not been met. These strains have been described as "reinforced" or of "exalted virulence" chiefly because of their behaviour on intracerebral (i.c.) inoculation into rabbits in which unusually short incubation periods may occur. With most, recently recovered, "street" viruses the first symptoms after i.c. inoculation are observed on the 14th to 17th day. With "reinforced" strains incubation periods as short as two to three days may be observed. However, in addition these strains are often associated with the absence of Negri bodies, greater resistance to divers methods of attenuation and greater pathogenicity for usually relatively resistant species of animal. Much less is known, or at least discussed, about the viruses which are "naturally" attenuated. The incubation period in the inoculated rabbit may be 30, 40, 50, 120, 150, or even 200 days. The duration of the disease in the inoculated animal, rabbit or guineapig, may be 8, 10, 13 or even 14 days, instead of only two to three days. Then cachexia may be observed in inoculated small laboratory animals instead of the paralytic or less common "furious" type of disease. This cachectic form has been recorded previously in guineapigs, Kraus observed it in rabbits inoculated with virus attenuated by passage in pigeons, and Lamb and McKendrick in rabbits inoculated subcutaneously with "fixed" virus.

Passage of virus from the nervous tissues of cachectic animals will give rise to the paralytic type of disease. Viruses "naturally" attenuated may fail to infect less susceptible species such as birds. They may also fail more frequently to induce symptoms in susceptible animals when applied to the scarified skin, conjunctiva and when injected by the nasal route. Their invasiveness is less and they exhibit greater sensitiveness to the action of physical and chemical agents. More curious, however, is their failure to "take" when inoculated into known susceptible species of animal. Thus, to give an example, a naturally attenuated strain of virus was inoculated into four rabbits, three guineapigs, a dog and a cat (intracerebrally). Only two guineapigs developed symptoms. Negri bodies may be regarded as cellular reactions. Their absence in the nervous system of rabbits inoculated with "reinforced" strains may be due to the fact that the cells have

[2]Remlinger (P.) & Bailly (J.). Les virus rabiques naturellement atténués.—*Ann. Inst. Pasteur.* 1942. Apr.–May–June. Vol. 68. No. 4–5–6. pp. 314–322.

not had sufficient time to react. In the case of small laboratory animals inoculated with naturally attenuated strains the Negri bodies are generally more widely distributed throughout the central nervous system, although they may not be abnormal in size. It must be remembered that the behaviour of a strain of virus experimentally in small laboratory animals may bear no relationship to the aggressiveness of the strain in man. Moreover a naturally attenuated strain of rabies virus may assume normal virulence on passage.

The difficulty of determining with exactitude between a "street" virus and a "fixed" virus is not easy although, as REMLINGER and BAILLY[3] state, it is sometimes desirable from either the scientific or the medico-legal aspect. A patient who is undergoing or who has undergone a course of injections with rabies vaccine may die following upon development of paralytic symptoms. Was death due to the effects of a street virus of exalted virulence, or on the other hand was it a case of "rage de laboratoire" (rabies produced by inoculation with laboratory products)? Inoculation of rabbits and dogs may not be very helpful since periods of incubation, symptomatology, histological findings (presence or absence of Negri bodies, Babes nodules, neuronophagia and infiltrative lesions in nerve ganglia) may be identical whether the infective agent is "fixed" or "street" virus. The authors have attempted to confirm the affirmation of Stanislaw LEGEZYNSKI [this *Bulletin*, 1939, Vol. 36, p. 725] that fixed virus does not undergo any modification of virulence by passage in mice while "on the contrary street viruses under the same conditions in the brain of white mice become avirulent after four to six passages, and mice inoculated intracerebrally survive." The present authors employed street viruses of divers origin, from Tangiers, Morocco and Gibraltar, and from horse, dog and ass. They experienced no difficulty in making 10–12 passages in white mice by intracerebral inoculation. The grey mouse *Mus musculus* behaved likewise. Not attenuation but an exacerbation of virulence of the street viruses was observed on passage through mice.

MASON[4] refers to the fact that it is known that the daughter strains of the original Pasteur (Paris) fixed strain of rabies virus differ from one another and from the parent strain in one or more attributes. In the same way street viruses may differ from one another in some respects. The author has estimated the virus potency (titre) of six strains of "fixed" virus for mice by intracerebral inoculation, the Pasteur (Paris) strain, and its daughter strains "Sassari" and "Tunis," (36, 30 and 32 passages respectively in mice prior to present investigations), a dog strain, L.T.W. "fixed" by mouse passage, S.K.L., a strain recovered from a skunk by mouse passage, and N.I.H., a strain maintained in guineapigs and rats (223, 6 and 6 passages respectively in mice before present experiments).

The m.c.l.d. (minimal cerebral lethal dose) of all six viruses lay between 10^{-4} and 10^{-5}. There appeared to be no difference between these "fixed" strains as regards antigenic potency in vaccination experiments. The author examined also 21 strains of "street" virus

[3]REMLINGER (P.) & BAILLY (J.). Il n'est pas possible de tirer des passages par la souris un caractère différentiel entre le virus rabique fixe et le virus de rue.—*Ann. Inst. Pasteur*. 1941. Sept. Vol. 67. No. 3. pp. 186–188.

[4]MASON (H. C.). A Comparative Study of the Behavior of Street and Fixed Viruses of Rabies in the Mouse.—*Amer. Jl. Hyg*. 1942. Sept. Vol. 36. No. 2. pp. 153–167. [17 refs.]

by experiments in white mice. Some of the strains appeared to be more invasive than others. Titre and invasiveness did not always run parallel. One strain with a m.c.l.d. of 10^{-2} killed mice more rapidly than did two strains with titres of 10^{-4}. Phenolized mouse brain vaccine given intraperitoneally protected mice against 10 to 100 m.c.l.d. inoculated intracerebrally. The same vaccine given subcutaneously protected mice against 1 to 10 m.c.l.d. He failed to demonstrate that hyperimmune rabbit serum could protect mice against intracerebral inoculation of either fixed or street virus.

Grysez[5] in passaging the Lille daughter strain of Pasteur (Paris) fixed rabies virus was impressed by the fact that in 70 per cent. of the inoculated rabbits the evolution of the disease was "normal," while in the remainder it was "abnormal." Thus during the period March 1939 to September 1940, 90 rabbits were inoculated; 68 showed a normal evolution of the disease (first signs 4th day, partially paralysed the 5th day, prostrate 6th day and 7th day, and dead 8th to 9th day) and in the other 22 the evolution was abnormal (deaths, one on 4th day, 5 on 5th day, 15 on 6th day, and 1 on 7th day). The 90 rabbits were inoculated in pairs: thus there were 45 pairs, in 29 of which the course of the disease was the same in the two rabbits of each pair (26 times normal and three times abnormal). In the other 16 pairs one rabbit behaved typically and the other did not. This in spite of the fact that, frequently, rabbits of the same weight were used in each pair. It was thought possible that the method of storage of the virus might be affecting it. Such factors as temperature of storage, 23°C. or 4°C., medium (buffered or unbuffered glycerine) and weight of rabbits, were investigated but no satisfactory explanation of the variations in incubation period in rabbits could be found. Biological variations unconnected with the weights of the rabbits might be responsible.

Remlinger and Bailly[6] point out that Chamberland and others many years ago recorded the antiseptic action of certain vegetable "essences." Recently Legroux recorded that the "essences" of mustard, cinnamon and rosemary destroy certain bacteria in fluid suspension in 24 hours, while respecting the diastases contained in the same emulsion. Bacteriophage behaved like diastase and not like bacteria. The present authors decided to test the effect of the vapour of eucalyptus, in closed jars at 21°C., on three viruses, those of rabies, equine encephalomyelitis (eastern strain), and Aujeszky's disease. Rabies virus was inactivated in 10 hours under these conditions, that of equine encephalomyelitis in 2½ days and that of Aujesky's disease in 5½ days. Control brain pulp smears were suspended in flasks at 21°C. in the dark without eucalyptus. Rabies virus was inactivated in 4 days, equine encephalomyelitis in 11 days and Aujeszky's disease in 19 days. There appeared to be a definite anti eptic effect of the eucalyptus on the viruses. *Bact. typhosum*, *Bact. paratyphosum A* and *B* were killed in two hours under similar conditions, whereas a sporulating microorganism like *B. subtilis* was not killed in less than three to four days. [Since the experiments were not done on a quantitative basis it may be that the apparent variable resistance of the three

[5]Grysez (Victor). Observations sur les causes modificatrices de l'évolution de la rage chez les lapins inoculés avec le virus fixe.—*Ann. Inst. Pasteur.* 1941. Mar. Vol. 66. No. 3. pp. 185–190. With 1 fig.

[6]Remlinger (P.) & Bailly (J.). Action de l'essence d'eucalyptus sur quelques ultravirus neurotropes.—*Ann. Inst. Pasteur.* 1942. July–Aug. Vol. 68. No. 7–8. pp. 428–430.

viruses could be explained by the different titres (virus potencies) of the test suspensions.]

Remlinger and Bailly[7] have previously recorded that neurones in the lung tissue may be infected with rabies virus. They considered that it would be interesting to determine whether mice could be infected with rabies by employing the common technique, in virus work in mice, of intranasal injection under anaesthesia. Nine of 27 mice contracted rabies when ether anaesthesia was employed and only one of 25 when the anaesthetic was not administered. In another experiment, virus was recovered from the lungs of mice which were killed shortly after an intranasal injection. It is concluded by the authors that the virus gained access to the central nervous system from the lungs. [This may be so. However it must be remembered that the anaesthetic in preventing sneezing, snorting and other expiratory movements also favours access of virus into the posterior nares and turbinates from which it may reach the olfactory lobes. Some of the injected virus may be swallowed.]

ii. *Diagnosis.*

Schaeffer and Leider[8] record the recovery of rabies virus from a case of fatal nervous disease of unknown origin. A man walked into a hospital and asked to be admitted for observation. He complained of difficulty in swallowing and attributed this to poisoning by some person unknown. Later he became wildly delirious and he died two days later. Abrasions were found on the hand and a healing wound on the finger. At autopsy, portions of nervous tissue were removed and placed in glycerine for subsequent examination for a possible virus infection. This material was stored, frozen at −76°C. later, and a suspension prepared and inoculated intracerebrally into six mice, two rabbits and two guineapigs. Bacterial contamination led to the death of the rabbits and guineapigs. Rabies virus was recovered from the inoculated mice. Negri bodies were demonstrated in the brains of mice, guineapigs and rabbits of subsequent passages. Serum neutralization tests with a known antirabies serum confirmed the diagnosis. The titre of the virus increased from 10^{-2} to 10^{-5} (limiting infecting dilution) in the 11th passage, and the incubation period diminished from nine days to six days. Subsequently information was obtained that the man had been bitten by his dog on the finger, the dog had had fits and then disappeared. Iodine was applied to the bite. The man's son was bitten on the leg on the same day, and iodine was also applied to the bite. Apparently nothing further transpired in the case of the boy.

Herzog[9] reports on what he describes as a reliable and rapid method of diagnosis for rabies. The method is not a new one and consists of the examination of the *ganglion nodosum* (ganglion of the trunk, inferior vagal ganglion or plexiform ganglion) of the vagus or pneumogastric

[7] Remlinger (P.) & Bailly (J.). Influence de l'anesthésie sur la transmission de la rage par voie pulmonaire.—*Ann. Inst. Pasteur.* 1941. Dec. Vol. 67. No. 6. pp. 465–466.

[8] Schaeffer (M.) & Leider (Ann G.). Recovery of Rabies Virus from the Brain of an Undiagnosed Case.—*Jl. Lab. & Clin. Med.* 1942. July. Vol. 27. No. 10. pp. 1263–1267. With 1 fig.

[9] Herzog (Ernst). Eine zuverlässige Methode zur schnellen Diagnose der Tollwut.—*Klin. Woch.* 1942. Aug. 22. Vol. 21. No. 34. pp. 749–752. With 4 figs.

nerve. The ganglion is more resistant to autolytic changes than the tissues of the central nervous system in which if only the head is received for examination it may sometimes be difficult to demonstrate Negri bodies. After fixing in 10 per cent. formalin, frozen sections are made and stained with a 1 per cent. watery solution of cresyl violet. After treatment with alcohol and xylol, sections are mounted in canada balsam and an observation can be recorded in about an hour. The tissue reactions consist of severe degenerative cell changes with tigrolysis and nuclear injury (cell shadows). There is also severe inflammatory infiltration (ganglionitis). There is also "neuronophagia" of the neurones and capsular cells, and leucocytic infiltration with formation of the nodules of van Gehuchten and Nelis. In silver preparations (*e.g.*, Bielschowsky-Gros) there is intracellular neurofibrillar thickening (Cajal and Garcia) but this method of staining is not essential.

[These lesions of the nerve ganglion, which have been described also in the spinal and sympathetic ganglia, cannot be considered, like Negri bodies, as specific to rabies since they may be seen in any infection of the nervous system due to a virus. The author has referred to cases in man, dogs, horses, cattle, cats, and swine in which it has not been possible to demonstrate Negri bodies ; in such cases it is suggested that the examination of the *ganglion nodosum* would be diagnostic. Now, to take the horse as an example, lesions in the spinal ganglia similar to those described in rabies have been observed in Borna disease [GALLOWAY, I. A., *System of Bacteriology*, Medical Research Council, 1930, Vol. 7, p. 347, H.M. Stationery Office, London]. But as already well recognized, their presence in an animal suspected to have been infected with rabies is of some aid to diagnosis, since their presence indicates infection of the nervous system. This may help to confirm clinical observations, especially if the c.n.s. is not in a suitable state for examination. The presence of nerve ganglionic lesions may be said to provide strong presumptive evidence of rabies if the history suggests it. The examination of the plexiform ganglion of dogs suspected to have died of rabies is a routine procedure at the Pasteur Institute, Paris, and it is a useful guide especially if the dog be young. VALLÉE showed that about a third of the old "normal" dogs which he examined had infiltrative lesions, and neuronophagia in the nerve ganglia, although to a less extent than in some dogs infected with rabies.]

iii. *Methods of Treatment and Statistics.*

It will be remembered that CUNNINGHAM, SHORTT and their coworkers found that the strain of fixed virus (ex Paris) in use in India was more antigenic than other strains of fixed virus of Indian origin [this *Bulletin*, 1933, Vol. 30, p. 581, and 1934, Vol. 31, p. 642]. HAMPIL and ROBERTS[10†] have now compared the immunogenic properties of 17 strains of fixed virus, using 21-day-old Swiss mice as the test animal. Immunity was tested by intracerebral injection of homologous virus. The results indicate that wide differences occur in the immunity response of the mice, depending on the strain of virus employed. Certain strains protected only against 1 to 20 m.l.d.

[10†] HAMPIL (Bettylee) & ROBERTS (G. H.). Investigations on the Immunogenic Properties of Fixed Rabies Virus Strains.—*Jl. Bacteriology*. 1942. Mar. Vol. 43. No. 3. pp. 397–407. [10 refs.]

whilst others protected against as many as 100 to 1,000 m.l.d., or even more, of the homologous virus. " The use of mice in the weeding out of non-antigenic vaccines is now an established procedure. . . . It seems not unreasonable to predict that killed vaccines prepared from a highly immunogenic strain will produce on repeated administration a greater degree of immunity to heterologous strains than those prepared from strains possessing low initial immunogenic properties. Studies along these lines are being continued."

A very remarkable non-virulent vaccine has been developed by WEBSTER and CASALS.[11†]

" Two months old beagle dogs are injected intracerebrally with mouse brain rabies virus, Pasteur strain. When the animals are prostrate, their brains are removed, weighed, triturated, and diluted with buffered distilled water to make a 5 per cent. emulsion. This emulsion is then centrifugalized at 500 r.p.m. for 5 minutes and the supernatant removed. This supernatant, to immunize, must titer at least 330,000 mouse doses per ml. and be relatively free of large particles. It is then rendered non-virulent by exposure to ultraviolet light for 35 minutes. Tests for sterility are made and the vaccine is then ready for use . . . . The vaccine can be prepared within 7 days, released within another 7 days, is relatively free from brain tissue, and appears quite harmless."

With regard to its properties, the authors cite experiments showing that the irradiated vaccine protects mice against 10,000 lethal doses, whereas a chloroform vaccine protected against 1,000, and a " widely advertised phenolized vaccine " gave no protection at all. It was found that a single dose of 0·1 ml. of irradiated vaccine is ample to immunize mice consistently against street virus injected intramuscularly. Post-infectional tests were carried out on groups of mice infected with 0·01 ml. of street virus into the gastrocnemius muscle, and given vaccine treatment commencing three hours later. " No phenolized vaccine has given a clear-cut protective effect ; chloroformized vaccines occasionally show some. The irradiated vaccine, however, in five doses totalling 0·5 ml., prevents rabies in most instances."

The final tests on dogs gave the following results :—

" Of 162 unvaccinated dogs injected with virus, about 84 per cent. died. Of 62 dogs given commercial phenolized vaccine 3 weeks prior to the test injection of virus, 72 per cent. died. Of 52 given chloroformized vaccine, 50 per cent. died. Of 35 given 30 to 40 ml. of irradiated vaccine in a single dose, all were protected save one ; of 24 given 5 to 10 ml. of the vaccine concentrated 6 times, all were protected."

WEBSTER and CASALS[12] have previously described experiments, the results of which showed that a vaccine containing at least 50,000 mouse intracerebral lethal doses (m.i.l.d.) of rabies virus rendered non-virulent by suitable irradiation with ultraviolet light will immunize mice, and that a vaccine containing 25,000,000 m.i.l.d. will immunize dogs against a subsequent test inoculation of rabies virus. In the present experiments the authors proposed to determine whether it was possible to immunize dogs with the required number of mouse doses of vaccine concentrated into a small volume and whether a single injection was adequate. The technique of the preparation of the

[11†] WEBSTER (L. T.) & CASALS (J.). An Improved Non-Virulent Rabies Vaccine. *Amer. Jl. Public Health.* 1942. Mar. Vol. 32. No. 3. pp. 268–270.

[12] WEBSTER (L. T.) & CASALS (J.). A Non-Virulent, Single-Dose Rabies Vaccine for Prophylactic Immunization of Dogs.—*Jl. Experim. Med.* 1942. Aug. 1. Vol. 76. No. 2. pp. 185–194.

vaccine is given in some detail : 2 months' old beagle dogs are injected intracerebrally with 0·5 cc. of a 1 : 10 dilution of dog brain virus material (Pasteur " fixed " strain). When the animals are prostrate they are killed, the brains are removed and ground in an electric mixer and diluted with distilled water containing 2 per cent. citric acid—sodium di-phosphate buffer (McIlvaine), *p*H 7·2 to make a 1 or 5 per cent. suspension. The suspension is centrifuged at 500 r.p.m. for 5 minutes and the supernatant fluid is removed. The supernatant should be relatively free from large particles to ensure that ultra-violet light will render the suspension avirulent. It must also titre, to at least 330,000 mouse doses per cc., *i.e.* prove fatal to Swiss mice when inoculated intracerebrally in 0·03 cc. doses and in a dilution of 10^{-4}. The material is rendered non-virulent by exposure to ultraviolet light for 35 minutes. [See HODES, WEBSTER and LAVIN, this *Bulletin*, 1941, Vol. 38, p. 161.] Tests for sterility are made, merthiolate in a dilution of 1 : 10,000 is added as preservative and the material stored in the ice box at 40°F. Dogs for tests are beagles four to six months old. In addition it has been necessary to include dogs of mixed small breeds of the same age. They are treated for worms on arrival and given 10 to 15 cc. of distemper serum, followed by one or two injections of distemper vaccine. The test inoculation of virus is 0·25 cc. of rabies virus deep into the neck muscles of each side. The authors conclude from their results that a single injection of non-virulent irradiated vaccine prepared as above will immunize dogs effectively against a subsequent test inoculation of rabies " street " virus and does so to a greater degree than do other vaccines now obtainable. The irradiated vaccine is easily and quickly prepared, keeps well and has a low nitrogen content. The question of whether the vaccine is more effective if given intraperitoneally rather than subcutaneously has not yet been definitely determined. In mice it is stated to be the route of choice for injection of vaccine. In dogs, however, it appears to be less convincing, and the authors' evidence suggests that there is little difference between the two routes. However, they favour the intra-peritoneal route, which they believe to be " slightly preferable." They state that they have unpublished evidence that the Pasteur strain of " fixed " virus is somewhat superior as an antigen to other strains of virus. [Since the efficacy of the vaccine is determined in some degree by the virus content it would appear to be difficult to appreciate the minimal dose of " concentrated " vaccine required to give adequate protection. When the titre of a 1 per cent. virus suspension employed for making vaccine indicated that it contained 3,330,000 m.i.l.d., 30 cc. of the vaccine given intraperitoneally to dogs gave them good protection. In another experiment a 5 per cent. virus suspension contained 33,000,000 m.i.l.d. and the vaccine prepared from this was concentrated six times at low temperature *in vacuo* ; 5 cc. of this vaccine given intraperitoneally gave good protection to dogs.]

ORTIZ ARMENGOL[13] reports that in 1935 there existed records covering 47 years of the work of the Antirabies Institute of Mexico. In 1937 the Institute was destroyed and these records were dispersed. The author, however, managed to secure records for a few years, and with this incomplete literature he has gathered together such data as he considered to be of interest. In 1928 LOPEZ replaced the Pasteur

[13]ORTIZ ARMENGOL (Federico). Breves consideraciones sobre la rabia en Mexico. *Rev. Méd. Yucatán.* 1942. Feb. 28. Vol. 21. No. 9. pp. 225–234.

vaccination method by a modification of the Semple method : a 4 per cent. suspension of rabbit cord in 0·5 per cent. phenol, incubated at 37°C. for 48 hours. The dose was 4 cc. instead of the original 2 cc. Three formulae are given for its application, presumably according to the severity of the case to be treated : (1) 14 doses of one per day, (2) 21 doses of two per day for five days then one per day, (3) 31 doses, three per day for five days then one per day. Since the introduction of the Semple method, the mortality diminished from three per 1,000 to 0 for 35,000 cases treated. Vaccination of dogs is also carried out with the following vaccine : 50 cc. physiological saline, 50 cc. glycerine, 1·25 cgm. phenol, 25 gm. brain and cord of rabbits inoculated with fixed virus, incubation at 37°C. for 72 hours. Dose, 4 cc. per kilo., inoculated subcutaneously into the flank. Up to 1935, 300,000 dogs were vaccinated, with a mortality rate of 14 per 100,000, as against the previous record of 7,800 cases of rabies in 10 years. The capture of stray dogs is also carried out. From 1939 to 1941, 4,575 dogs were captured. Control of rats is advocated also. During the same three years in 364 cases, bites were due to rats. It is interesting to note also that in 1932, of 18 rats caught in the garden of Cartagena, Tacubaya, six were proved to be infected with rabies by inoculation of rabbits. Stress is placed also on the necessity for the routine inspection of dogs in premises. It is not always realized that dumb or paralytic rabies is often overlooked. Owners frequently attempt to handle and treat cases with dysphagia believing the symptoms to be due to a bone stuck in the throat. If they have injuries or scratches on the hand, or these are produced during the examination, the risks are obvious. The rest of the paper deals with statistics, etc.

Cruveilhier and Viala[14] report on the antirabies vaccinations, carried out by the Pasteur Institute, Paris, during the year 1940, according to the plan established at the International Rabies Congress ; 1,196 persons presented themselves for treatment and it was considered that 449 of these should receive vaccine. The method of treatment, which is already well known, is given in detail ; the method is that of Pasteur. The cords are dried in flasks in a dark room at 22°C. over caustic potash. After 2, 3 or 4 days of desiccation the cords are placed in small bottles containing sterilized neutral glycerine. The vaccines thus prepared are kept at 3°C. in the ice chest. The cords are no longer used for vaccination if they have been in glycerine more than 10 days. Each day the patients receive 4 to 5 mm. of cord in 3 cc. of physiological saline. Treatment lasts 15, 18, 21 or 25 days, according to the severity of the bites. On December 31st, 1940, the "fixed" virus employed had been passaged 1,670 times since it was first employed in the antirabies service in "rue Ulm." The cords are removed from the rabies-infected rabbits by Oshida's method. The rabbits are killed and bled as soon as paralysis is complete so as to avoid possible secondary bacterial contamination. 254 of the treated patients were bitten by stray dogs, 43 by stray cats, 106 by dogs and 35 by cats with known owners, 10 by rats and one by "another animal."

Four hundred and forty-one of the patients belonged to Category C, *i.e.* the animal responsible for biting was suspected of rabies, the

[14]Cruveilhier (L.) & Viala (Ch.). Les vaccinations antirabiques à l'Institut Pasteur en 1940.—*Ann. Inst. Pasteur.* 1941. June. Vol. 66. No. 6. pp. 483–488.

remaining eight belonged to Category B, *i.e.* rabies had been diagnosed by the clinical picture in the dog or cat. In 12 of the cases of category C, a histological examination of the plexiform ganglions (*ganglion nodosum*) revealed infiltrative lesions as seen in the early stages of infection of the nervous system by a virus such as rabies. In 396 cases the bites inflicted were deep and in 289 cases no clothing protected the bitten person. In 316 cases the bites were about the head or upper limbs.

255 cases were treated within 4 days after the bite.
95 cases were treated within 5 to 7 days after the bite.
63 cases were treated within 8 to 14 days after the bite.
18 cases were treated within 15 to 21 days after the bite.
18 cases were treated more than 21 days after the bite.

In none of the 449 cases treated were any untoward effects recorded, *i.e.* no cases of post-vaccinal paralysis and no deaths. A table is given as usual showing the results of vaccination since the procedure was first instituted in 1886. Since 1925 no fatal cases following vaccination have been recorded.

YEN[15] has re-examined the possibility of experimental sero-prophylaxis in mice. Contradictory results have previously been reported. "Certain workers have reported the prolongation of the percentage survival over untreated controls." The control of the weight and age of the test animals is important in such experiments as also are the dosage of virus, the route of infection, the quantity of serum in antiviral units, and the interval between virus infection and antiserum administration. The observations reported indicate the beneficial effects of a single dose of antiviral serum against many fatal doses of rabies virus. Fixed rabies strain (Habel) was employed and maintained by frequent intracerebral passage in mice. Sera were prepared from rabbits by intra-abdominal inoculation of 5 cc. doses of a phenol treated vaccine given twice weekly for the first four weeks followed by similar injections with a live vaccine for four to six weeks. The live vaccine was a 10 per cent. suspension of brain from rabbits dying on the 8th to 10th day after rabies infection. The phenol-treated vaccine consisted of a similar suspension containing 0·5 per cent. phenol and incubated at 37°C. for 48 hours. All vaccines were employed within two weeks after preparation. The antisera employed contained $3{\cdot}3 \times 10^4$ antivirus units and these were kept in the frozen state without antiseptic, in a refrigerator. The author concludes that the administration of a single dose of potent antirabies serum given intraperitoneally 10 to 15 minutes after infection with virus is capable of prolonging the life span of intracerebrally infected mice, and saving the lives of some intramuscularly inoculated mice depending on dosage of serum and amount of virus given. The combined use of vaccine and antiserum afforded full protection to the mice tested with 100,000 minimal cerebral lethal doses of virus.

iv. *Paralytic Accidents.*

A case described as acute myelitis following antirabies vaccination is recorded by DANG.[16] He had seen only this case during a period of

[15] YEN (C. H.). Protective Value of Antiviral Serum in Experimental Rabies Infection.—*Proc. Soc. Experim. Biol. & Med.* 1942. Apr. Vol. 49. No. 4. pp. 533–537.

[16] DANG (M. L.). Acute Myelitis (Post Anti-Rabic Inoculation.)—*Indian Jl. Med. Assoc.* 1942. Mar. Vol. 11. No. 6. pp. 173–174.

20 years in practice. He states that there was an "acute transverse lesion of the cord and no lesions elsewhere in the nervous system." There was abdominal pain, vomiting and general discomfort including a burning sensation all over the body, pain in the back over the dorsal spines of the sixth and seventh vertebrae, and constipation. These symptoms were observed on July 27th, 1941, *i.e.* after six daily injections had been given. Later, July 29th, 1941, there was retention of urine, a slight temperature rise and symptoms of paralysis of the lower extremities. These persisted till August 20th, 1941, when the paralysis completely disappeared. There was no further record of any disturbance except that the bladder condition took a long time to clear up.

The first case of postvaccinal paralysis since the introduction of a carbolized rabies vaccine (Semple) in May 1938, is reported from Vienna by PIRINGER[17].

Vaccination Method	No. of cases treated	Fatal cases of rabies.	Cases of Myelitis.	
			No.	Per cent.
Pasteur & Alivisatos 1919–Sept. 1923 ...	2,488	17	30	1·2
Högyes & Alivisatos I. Oct. 1923–1926 ...	1,934	3	4	0·21
Högyes & Alivisatos II. 1934–1937	1,750	3	3	0·22
Semple May 1938–Aug. 1941	1,249	0	1	0·07

As seen from the above table (which omits records for the period 1926–1934), before this date a combination of other methods of vaccination had been employed. The Semple vaccine has given good results, the fatal cases of rabies have diminished, and also the number of cases of postvaccinal paralysis.

v. *Rabies in Animals.*

FRANKLIN[18] stresses the undesirability of animals susceptible to rabies being kept as pets by military personnel in countries where the disease is prevalent. He gives the history of an outbreak involving two dogs and a cat kept as pets. Soldiers had to be treated with vaccine after being bitten by one of the dogs. The cat also attacked a human being before it was destroyed. The diagnosis of rabies was confirmed by biological tests.

[17] PIRINGER (Walter). Myelitis post vaccinationem contra lyssam nach der Methode von Semple.—*Zent. f. Bakt.* I. Abt. Orig. 1942. Mar. 26. Vol. 148. No. 7/8. pp. 321–331. [28 refs.].

[18] FRANKLIN (A. V.). An Outbreak of Rabies.—*Jl. Roy. Army Vet. Corps.* 1942. Aug. 18. Vol. 13. No. 4. pp. 121–122.

vi. *Miscellaneous.*

Levaditi[101] reports experiments upon the association of herpes and the street virus of rabies. When a mixture of the two viruses is inoculated intracerebrally into mice, the two viruses persist through one or two passages. Then the rabies virus becomes less apparent and finally disappears. The reason of this according to the author is that the virus of herpes destroys the neurones, and so prevents the formation of Negri bodies.

Levaditi[80] and his collaborators have reported previously on the results of inoculating mixtures of two different viruses intracerebrally into mice. Thus they found that if a mixture of herpes and rabies viruses was inoculated into mice the virus of herpes supplanted that of rabies on further passage. On the other hand the viruses of rabies and lymphogranuloma inguinale can exist side by side, if a mixture is inoculated intracerebrally into mice, perhaps because these two viruses have somewhat different tissue cell affinities. In the present limited experiments a mixture of the virus of louping ill and rabies "street" virus was inoculated intracerebrally into mice. The strain of street virus employed was Bucarest 11 and it was stated to be a strain associated with the formation of Negri bodies in the c.n.s. of inoculated mice (somewhat loosely described as "Negrigenic"). The virus of louping ill "produces an intense encephalitis" and "attacks nerve cells in the *Cornu Ammonis*." On the basis of histological examination alone the author concluded that louping ill virus supplanted that of rabies when further passages were made. No Negri bodies were seen. [It is surely rather hazardous to draw conclusions from histological evidence only. It is known, for example, that the attribute of a strain of rabies virus to "produce" Negri bodies can be lost under certain circumstances. Furthermore, this result may have been obtained because of a disproportion in the relative amounts of each virus in the mixture.]

Aujeszky's Disease.

The virus of Aujeszky's disease readily infects the chorio-allantoic membrane of the developing chick embryo, and produces pocks which may coalesce to form ulcers. Since the virus of Aujeszky's disease produces a rapidly destructive encephalitis in a wide variety of animals, Bang[21] considered that a selective effect of the central nervous system of the chick on the virus was to be expected. He found that all four strains of virus of Aujeszky's disease studied had a marked neurotropism in the chick embryo. The four strains employed were: (1) a Hungarian strain sent to Shope in 1931, (2) Iowa A strain 1930 recovered by Shope from cattle. Both 1 and 2 were "fixed" or old-established strains, in that they had been passaged in rabbits more than 50 times. Strain (3) Iowa B—Shope, and (4) a swine strain—recovered by Ray from swine in Nebraska, had been passaged in rabbits only 15 and 5 times respectively and are referred to as "field"

[101] Levaditi (C.). Association entre ultravirus. Herpès et rage des rues. *C. R. Soc. Biol.* 1942, Apr. Vol. 136, No. 7–8, pp. 331–332.

[80] Levaditi (C.). Association entre ultravirus, rage et louping-ill.—*C. R. Soc. Biol.* 1942 July. Vol. 136, No. 13–14, pp. 474–475.

[21] Bang (Frederick B.). Experimental Infection of the Chick Embryo with the Virus of Pseudorabies.—*J. Experim. Med.* 1942 Sept. 1. Vol. 76, No. 3, pp. 263–270. With 7 figs. on 2 plates. [26 refs.]

strains. All four strains after being cultivated in eggs produced one or more of the following conditions: (1) Fatal encephalitis when inoculated intracerebrally into rabbits. (2) Pruritus when inoculated subcutaneously into guineapigs and rabbits. (3) Pock lesions on chorio allantoic membranes were neutralized by hyperimmune swine serum. (4) Intranuclear inclusions in chick embryos. When 12-day embryos were used there were scattered pocks on the chorio-allantoic membrane, and with greater concentrations of virus large ulcers were seen. Lesions on the membrane were followed by infection of all tissues of the central nervous system of the embryo. The "fixed" or old-established strains produced a hemorrhagic destruction of the embryo brain referable to the action of the virus on the endothelium of the blood vessels. No neuronophagia was observed in the c.n.s. Intranuclear inclusions indistinguishable from those of herpes were found in all nerve cells, not only the neurones but in cells of the meninges, choroid plexus and of the retina in some cases. There was also some infiltrative neuritis with polymorphonuclears. This widespread destruction of the c.n.s. of chick embryos has not been reported previously. "Field" strains lacked the tendency to produce haemorrhagic reactions in the embryo brains but when seeded on to the chorio-allantoic membranes they infected the nervous tissue. The reaction of the chick embryos to the virus varied with the age of the embryo, as regards the development of encephalitis following upon the membrane lesions. Thirteen-, 15- and 18-day embryos were inoculated and also two day old chicks. *Thirteen-day embryos* (16 day when fixed) showed large ulcers and confluent pocks with low dilutions of virus, nerve tissues extensively involved and haemorrhagic lesions prominent; *15-day embryos* (20-day when fixed), 5 to 10 scattered pocks on membranes. Many nerve cells were destroyed but there was no haemorrhagic reaction; a few leucocytes penetrated the brain tissue; *18-day embryos*, no visible lesions on the chorio-allantoic membrane—encephalitis of non-haemorrhagic type; *two-day-old chicks*, some developed encephalitis in six days, no haemorrhagic reaction, only slight nerve cell destruction, perivascular polymorphonuclear infiltration and neuronophagia with mononuclear infiltration. Glial nodules were seen also. *T. A. Galloway.*

Johnson (H. N.). **Significance of the Negri Body in Diagnosis and Epidemiology of Rabies.** *Illinois Med. Jl.* 1942. May. Vol. 81. p. 382. [Summary taken from *Jl. Amer. Med. Assoc.* 1942. Aug. 1. Vol. 119. No. 14. p. 1138.]

According to Johnson, Negri bodies cannot always be found in man and animals dying of rabies. It is necessary to resort to animal inoculation when the microscopic examination of a brain specimen is negative. All brain specimens received at the Georgia State Health Department in 1937 for the diagnosis of rabies were examined microscopically, and those found negative were studied by mouse inoculation. Of the 771 specimens found positive for rabies, 10·5 per cent. were Negri negative. In an epizootic of fox rabies, 137 brain specimens were positive for rabies by mouse inoculation and 9·4 per cent. of these were microscopically negative. An analysis of 92 mouse positive brain specimens obtained in Alabama from dogs that had been vaccinated one month to one year before the onset of rabies demonstrated that 14 per cent. were Negri negative. When dogs were experimentally infected with rabies by intramuscular inoculation,

39·7 per cent. of the animals were negative by microscopic examination. Forty-six per cent. of the dogs developing rabies were vicious at some time during the course of the disease. Only 21·4 per cent. of these were Negri negative as compared with 52 per cent. for the dogs with paralytic rabies. This partially explains the discrepancy between the Negri findings in natural and experimental rabies, as the majority of routine specimens are from vicious and biting dogs. The duration of symptoms before death is correlated to the absence or abundance of Negri bodies. Vaccinated dogs dying of rabies exhibited the same clinical course as unvaccinated controls, and the error in microscopic diagnosis was approximately the same in the two groups. The studies suggest that rabies street virus is altered in either virulence or manner and site of multiplication during epizootics of the disease, and at this time a higher proportion of the infected animals will be Negri negative. The rapid microscopic diagnostic method of Sellers is recommended. The indications for animal inoculation of brain specimens are enumerated, and the white mouse is recommended for the purpose.

KUBES (Vladimir) & GALLIA (Francisco). Estudios inmunológicos sobre la pluralidad de los virus rábicos en Venezuela. [**Immunological Studies on the Plurality of Rabies Viruses in Venezuela.**]—*Bol. Inst. Investigaciones Vet.* Caracas. 1942. Jan. Vol. 1. No. 1. pp. 1–45. [11 refs.] English summary.

"From an epizoölogical standpoint, there are in Venezuela two kinds of rabies: one of a sporadic character, occurring chiefly among carnivores (dogs and foxes) and occasionally among other animals (cattle); another of a distinctly enzootic character, peculiar to cattle and called *paralytic rabies*. While the former seems to have a genuinely canine origin, in the spread of the latter the vampire bat (*Desmodontidae*) plays a part.

"In view of these etiologic-epizoölogical differences, the writers undertook studies of an immunological character, availing themselves, to this effect, of the Habel test (slightly modified) for the titration of anti-rabies vaccines.

"According to his method, mice immunized with 6 intraperitoneal injections of the anti-rabies vaccine on test receive then, by the intracerebral route, the rabies virus in serial tenfold dilutions (1 : 10, 1 : 100, 1 : 1,000, etc.). By injecting simultaneously, and with higher dilutions, non-immunized control mice, one is able to determine, to a fair degree of accuracy, how many lethal doses of the virus the vaccinated animals have withstood.

"Now, using this method in cross-immunity tests of several vaccines or rabies viruses, as the writers did, it is relatively easy to find out whether there are any immunological differences.

"In addition to the cross-immunity tests, the writers also carried out neutralization tests *in vitro* with antisera obtained from mice discarded from the Habel tests (mice which, following immunization, withstood the intracerebral inoculation of the homologous virus). In order to assure a greater accuracy in this test, it is necessary to determine simultaneously, besides the minimum neutralizing dilution of the antiserum on test (using it in several serial dilutions, but mixed always with an equal amount of virus of the same concentration), the minimum lethal dilution of the examined virus.

" In all, 6 rabies viruses were investigated, 5 native ones and the sixth a *Pasteur* fixed-virus strain from the Rockefeller Institute. Of the 5 native viruses, 3 were isolated from cattle affected with paralytic rabies (States of Bolivar and Miranda), and the 2 remaining ones from sporadic cases in a canine and a bovine in the State of Táchira. The bovine is supposed to have been bitten by a rabid dog.

" Two of the Venezuelan viruses (both from paralytic rabies cases) already had, when investigated, fixed-virus characteristics, due to their having undergone numerous passages through bovines (fixed *Bolivar* virus, with 95 passages, and fixed *Miranda* virus, with 76 passages), whereas the three remaining ones were street viruses.

" The anti-rabies vaccines used for this purpose have been two: (1) a *Pasteur* vaccine made from the above-mentioned *Pasteur* virus, and (2) a Bolivar vaccine prepared from the *Bolivar* virus referred to. In both of them were used brains and cords from bovines killed at the climax of the disease, the final product being a 15% suspension of brain and cord in 1% phenolized saline solution. After remaining 3 weeks in the cold room, the vaccines were ready for use.

" The results obtained in this research may be summed up as follows:

" 1. By means of the Habel test, originally intended to determine the protective power of anti-rabies vaccines, the plurality of rabies viruses in Venezuela has been established.

" 2. The Habel test, by virtue of its high sensitivity, has proved to be most suited for carrying out immunological studies of this nature.

" 3. Five native viruses, immunologically compared with a *Pasteur* virus strain, split into two biologically different groups: one consisting of viruses with antigenic properties resembling those of the *Pasteur* virus, and another composed of viruses resembling each other, but differing from the former group.

" 4. The writers assume that this biological difference, or plurality of the Venezuelan rabies viruses, is due to their different source. In effect, while the Pasteur group was made up of genuinely canine viruses, in the other group appeared only viruses proceeding from paralytic rabies cases, supposed to be spread by bats.

" 5. The chief immunological difference between the two groups rests on the fact that, while the *Pasteur* vaccine has conferred a most satisfactory protection against the *Pasteur* group viruses (canine), it has almost completely failed with regard to paralytic rabies viruses (supposed to come from a bat source). On the contrary, the vaccine prepared from fixed native virus of paralytic rabies (*Bolivar* virus) has shown a polyvalent antigenic action on all the six viruses investigated, whether fixed, street, canine or of paralytic rabies.

" 6. The one-sided action of the *Pasteur vaccine* might be explained in the writers' opinion, by the modification which the *Pasteur* virus may have undergone after so many rabbit passages, to the extent of acquiring really specific characteristics. Hence the vaccine made from it acts, first of all, on the homologous virus and also, naturally, on kindred viruses, such as the canine, while it does not protect against the paralytic rabies virus (bat source), which is biologically more distant. On the contrary, the *Bolivar* virus, either by its special antigenic

properties or by its relatively few passages and, consequently, lesser differentiation, developed a wider action of a polyvalent character.

"7. The serum-neutralization tests *in vitro* gave results much resembling those of the cross-immunity tests.

"8. It has been established that sera of mice newly-discarded from the Habel tests for the titration of anti-rabies vaccines, are most suited for serum-neutralization tests *in vitro*.

"9. The discrepancies between the present findings and those of preceding workers, which did not disclose any biological difference between the canine rabies virus and the paralytic rabies virus, are explained, in the writers' opinion, by the dissimilarity of the methods made use of.

"10. Finally, there arises the need of fighting paralytic rabies in tropical countries by means of vaccines prepared from fixed paralytic-rabies virus, or, even better, fixed native virus."

MALARIA.

DUREN (A.). Contribution à l'étude du paludisme endémique au Congo Belge, district du Kwango. [**Contribution to the Study of Endemic Malaria in the Kwango District of the Belgian Congo.**] — *Ann. Soc. Belge de Méd. Trop.* 1940. Sept. 30. Vol. 20. No. 3. pp. 265–271.

This paper records the results of the blood examination of 752 inhabitants of four villages on a plateau 900 to 1,000 metres high, between the rivers Wamba and Inzia, and between latitudes 6° and 7° S. Thick drop preparations were alone examined. Very few of the native children of this region present obvious signs of chronic malaria. Malaria parasites were found in 33·6 per cent. of the bloods. In the first year of life only 6·25 per cent. of infants harboured parasites. Thereafter the parasite index increased, attaining its maximum, 45 per cent., in the age group 11 to 20 years. No parasite was found in the eight persons over 50 who were examined. These figures indicate that there is but little local infection in the villages. Nearly all the Anopheles caught in the huts were *A. dureni*, Edwards. Many infections may have been contracted in the Inzia Valley which is below the altitude of 600 meters.

P. falciparum is by far the most prevalent species; it was found alone in 222 of the 252 positive preparations, and in combination with *P. malariae* or *P. vivax*, or both, in 16 others. *P. vivax* was found alone only twice; in combination with other species nine times. *P. malariae* was the only species seen in 12 thick smears; in combination with other species it was seen nine times. There were two triple infections. Gametocyte carriers numbered 72.

No trypanosomes or spirochaetes were seen in any of the bloods examined. Microfilariae were frequently seen, probably *Acanthocheilonema perstans*. *Norman White.*

Schwetz (J.) & Baumann (H.). Contribution à l'étude du paludisme endémique dans le district du Kwango (Congo Belge). [**Contribution to the Study of Endemic Malaria in the Kwango District of the Belgian Congo.**]—*Ann. Soc. Belge de Méd. Trop.* 1940. Sept. 30. Vol. 20. No. 3. pp. 345–353.

Two previous papers dealing with malaria in the Kwango District have been published. Schwetz & Geronnez found that *P. falciparum* and *P. malariae* were almost equally prevalent. Lamote found only *P. falciparum* infections [this *Bulletin*, 1939, Vol. 36, p. 778; 1940, Vol. 37, p. 126]. In the present paper the authors record, in very great detail, the results of their examination of thick drop blood preparations obtained from 353 natives of four villages between the Lukula and Luie Rivers, from which neighbourhood Lamote obtained his material. As elsewhere in the Lower Congo the proportion of infants and young children harbouring malaria parasites is very high; the parasite rate then decreases with increasing age. The gametocyte indices were very low. Parasites were scanty in nearly all smears, except in those from young children. *P. malariae* was found but not frequently. In one village, in which the infection rates were lowest, *P. malariae* was not found at all. The authors cite this as a warning against attaching too great importance to results obtained by random sampling. *Norman White.*

Schwetz (J.) & Baumann (H.). Quelques données sur le paludisme endémique dans l'agglomération de Stanleyville en 1939. [**Certain Facts regarding Endemic Malaria in Stanleyville in 1939.**]—*Ann. Soc. Belge de Méd. Trop.* 1940. Sept. 30. Vol. 20. No. 3. pp. 355–370.

Between 1928 and 1932 the authors carried out several inquiries into malaria prevalence in Stanleyville, the results of which were duly published [this *Bulletin*, 1930, Vol. 27, p. 644; 1934, Vol. 31, pp. 418, 474]. Since then, until the appearance of this paper, nothing further has been published on the subject. A Health Service was established in Stanleyville in 1932, since when it has devoted much attention to the mechanical prophylaxis of malaria.

In 1939 examination was made of the blood of 109 infants up to 2 years of age at the Infant Welfare Centre of Stanleyville, and of 348 scholars aged 6 to 15 years, at the School *des Frères Maristes*. The results of these examinations are compared with those obtained in the same institutions 7 to 11 years earlier.

The parasite index of the infants, 51·3 per cent., was appreciably lower than in 1931 and 1932, when it was 83 and 87 per cent., but the proportion of children harbouring gametocytes was almost the same, 40 and 48 per cent. In a third of the positive films *P. malariae* was found in association with *P. falciparum*, the predominant parasite. *P. vivax* was not found at all in 1939 though in 1931 and 1932 it was found in 3 and 4 per cent. of positive bloods.

The parasite index of the scholars was 94·2 as compared with 87·8 in 1928. That parasites were very few is shown by the fact that had thin smears alone been examined the parasite rate would have been but 25·5. *P. malariae* was found in 9 per cent. of the positive bloods. A few *P. vivax* were found five times; none was seen in 1928. The scholars had an appreciably lower gametocyte rate than 11 years previously.

On the whole there has been little change in the malaria endemicity of Stanleyville. *Norman White.*

Schwetz (J.). Sur une épidémie mystérieuse, suspecte et soupçonnée de paludisme, constatée dans une agglomération indigène d'un trés haut plateau du Ruanda. [**Mysterious Epidemic, Suspected Malaria, among the Native Population of a very High Plateau of Ruanda.**]—*Ann. Soc. Belge de Méd. Trop.* 1941. Mar. 31. Vol. 21. No. 1. pp. 36–61. With 2 maps.

A plateau some 1,900 metres above sea level, rising above the southern shore of the small Lake Luhondo, in the northern part of Ruanda very near the Uganda frontier, and between that frontier and Lake Kivu, is the scene of the incident described in this paper. In 1938 and 1939 a notably increased mortality was reported among the native inhabitants on this plateau. A medical officer carried out investigations on three occasions and came to the conclusion that malaria was responsible for the increased morbidity and mortality. He found malaria parasites in the blood of a high proportion of the sick. In September 1939 the author of this paper carried out an inquiry. He was very sceptical as to the possibility of malaria being responsible for an epidemic at such a high altitude ; no vector species of Anopheles have ever yet been found on these high plateaux. His findings are fully reported. The only Anopheles found breeding were *A. mauritianus* var. *paludis* and *A. christyi*, neither of which has ever been incriminated as a serious vector of malaria. Of 106 children under 15 years of age examined only seven had any splenic enlargement, and in these cases the enlargement was but slight. The blood of 225 individuals was examined. Malaria parasites were found in 25, of whom 15 were children under 10 years of age. Seven of the positive findings were among 32 individuals who had reported sick. *P. malariae* was responsible for just over half the infections, *P. falciparum* for the remainder ; *P. vivax* was not seen. Quartan gametocytes predominated. There was not a single heavy infection, and no microscopic evidence of acute malaria. But there was a feeble proportion of infection among all age groups examined. It would seem that malaria was not responsible for the epidemic, but no explanation is forthcoming as to how the women and children on this high plateau, who are not known to have visited endemic areas, acquired their infections. It is hard to understand how they could have acquired an immunity or tolerance to malaria. *Norman White.*

Schwetz (J.), with the collaboration of H. Baumann. Recherches sur le paludisme dans les camps miniers de la division de Kadubu-Mufwa de la Minière des Grands Lacs (M.G.L.) et dans les camps miniers du secteur de la Lubimbe du Comité National du Kivu (C.N.Ki.), (District du Kivu). [**Researches on Malaria in the Mining Camps of the Kadubu-Mufwa Division of the Surface-Mine of the Great Lakes (M.G.L.), and in the Mining Camps of the Lubimbe Sector of the National Committee of Kivu (C.N.Ki.), in the Kivu District.**]—*Ann. Soc. Belge de Méd. Trop.* 1941. June 30. Vol. 21. No. 2. pp. 87–129. With 1 map.

These two collections of mining camps, some 30 kilometres apart, lie 90 to 100 kilometres south-west of Costermansville on the southern

shore of Lake Kivu. In the Kadubu group (M.G.L.) both *A. gambiae* and *A. funestus* occur and there is severe endemic malaria. Blood examinations were indicative of this. Many of the labourers come from the Ngweshe region, which is free from malaria. It might be expected that these would suffer from acute, even epidemic, malaria. Such outbreaks had, indeed, been reported, but when the inquiry was undertaken most of the miners had been present two or three years and had apparently attained a state of premunition. The mining camps of the Lubimbe sector of the C.N.Ki. are at a higher altitude, anophelines are rare and malaria endemicity is but feeble. The findings are set out in very great detail. *Norman White.*

i. VAN WYMEERSCH (H.). Contribution à l'étude du paludisme dans un groupe de collectivités indigènes du Congo Belge. (Villages de la rive gauche du fleuve Congo en amont de Léopoldville.) [**Malaria in Native Villages on the River Congo above Leopoldville.**] —*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 81–85. With 1 map.

ii. TROLLI (G.). Endémie malarienne au Chenal d'apres les examens microscopiques et les tableaux statistiques du Dr. van Wymeersch. [**Endemic Malaria in Chenal according to the Microscopic Examinations and Statistical Data of Dr. van Wymeersch.**]—*Ann. Soc. Belge de Méd. Trop.* 1941. June 30. Vol. 21. No. 2. pp. 131–166. With 1 map.

These two papers contain accounts of the same work. Dr. van Wymeersch of the Foréami (*Fonds Reine Elisabeth pour l'Assistance Medicale aux Indigènes du Congo Belge*) examined the blood of all the inhabitants of the villages on the left bank of the Congo from Kwamouth, where the Kasai joins the Congo, to Stanley-Pool, making 3,178 examinations. The author of this paper rearranges and comments on the findings. The population is mobile and floating. Cutting firewood for river steamers and fishing provide occupation for the men, the cultivation of manioc for the women. There is no scarcity of food but sleeping sickness is rife (2·7 per cent. infected). The population is declining. This would appear to be the case from the constitution of the population (3,178) examined: adult males 34·7 per cent.; adult females 33·4; children aged 0 to 3, 7·2; children aged 3 to 15, 24·6 per cent. The thick drop method of blood examination was used throughout.

Of the 3,178 examined 45·56 per cent. were infected with malaria. The parasite indices were: children 0 to 3, 90·4; children 3–15, 64·5, and adults 33·9 per cent. In 747 of the 1,448 positive cases schizonts were rare. *P. falciparum* gametocyte carriers represented 15·5 per cent. of the population. Quartan parasites were found in 99 persons, 72 of whom had mixed infections. No *P. vivax* was identified.

Norman White.

SCHWETZ (J.), with the collaboration of H. BAUMANN, Mme. BEUMER & M. FORT. Sur le paludisme endémique constaté dans six agglomérations indigènes du Bas-Lomami (Congo Belge). [**Endemic Malaria found in Native Villages on the Lower Reaches of the Lomami River (Belgian Congo).**]—*Ann. Soc. Belge de Méd. Trop.* 1942. Mar. 31. Vol. 22. No. 1. pp. 45–71. With 1 map.

The villages concerned in this report are situated on either side of the last 250 km. of the Lomami River before it joins the Congo at Isangi,

west of Stanleyville. This area lies between 1° S. and 1° N. of the Equator. The medical service of this part of the Belgian Congo was entrusted in 1937 to Cemubac (Medical Centre of the Brussels University). The anopheline fauna is almost restricted to the ubiquitous *A. gambiae*. A very few *A. funestus* were captured, and in one place specimens of *A. marshalli* var. *moucheti* were found. Thick drop preparations and blood smears were made from 812 native inhabitants of various age groups living in six widely separated centres of population. The results of these blood examinations are set out in minute detail. The parasite rate of children varied from 85 to 94 per cent.; of adults from 30 to 46 except for one inhabited locality where it was as low as 20. The gametocyte index was 52 per cent. for children and 15 for adults. These figures are fairly representative of hyperendemic malaria conditions as they are found in Central Africa. *P. vivax* is very rare; one solitary adult *vivax* infection was noted. *P. malariae* is very common in children and is nearly always found in association with *P. falciparum*; it was very rarely found in adults.

The proportion of persons infected with microfilariae is extremely high. *W. perstans* is much more common than *L. loa*. *Onchocerca volvulus* was largely confined to the members of a tribe, the Mukuma, in an area some 200 kilometres from the Congo. *Simulium damnosum* is common; *Simulium medusaeforme* was also found. *Culicoides grahami* is a very troublesome pest in some localities.

Norman White.

Emmel (L.), Jakob (A.) & Gölz (H.). Elektronenoptische Untersuchungen an Malaria-Sporozoiten und Beobachtungen an Kulturformen von *Leishmania donovani*. [**Electronoptical Observations of Sporozoites of Malarial Parasites and of Culture Forms of *L. donovani*.**]—*Deut. Trop. Ztschr.* 1942. July 1. Vol. 46. No. 13. pp. 254–258. With 9 figs.

The authors have made observations on the sporozoites of malarial parasites and the culture forms of leishmania by means of the electron microscope. They find that the sporozoites have one end more pointed than the other, and that those of *P. falciparum* are less uniform in size than those of *P. vivax*. Evidence was obtained of the existence of a definite periplast. Certain other appearances were difficult to interpret. As regards the flagellate forms of *L. donovani* it was noted that the flagellum was extraordinarily thick and that it ended abruptly. The cytoplasm showed clear and dense areas indicative of a vacuolated structure. Microphotographs illustrate the various findings.

C. M. Wenyon.

Rodhain (J.) & van Hoof (M. Th.). Recherches sur l'anophélisme en Belgique. [**Researches on Belgian Anopheles.**]—*Ann. Soc. Belge de Méd. Trop.* 1942. Mar. 31. Vol. 22. No. 1. pp. 19–43. With 1 map. [25 refs.]

The authors present a careful account of what is known of the former prevalence of malaria in Belgium. They are doubtless correct in thinking that it was transmitted by *Anopheles maculipennis atroparvus* and not by *messeae*, the only other variety which occurs. *A. m. atroparvus* is found in Belgium not only in slightly brackish waters in the coastal region of Western Flanders and in polders (*i.e.* land reclaimed from the sea) in the province of Antwerp, but also in certain inland localities in which the water is quite fresh.

P. A. Buxton.

Gasperini (G. C.). La fauna anofelica della Piana di Selaclacà (Tigrai Orientale). [**The Anopheles of the Plains of Tigre.**]—*Boll. d. Soc. Italiana di Med. e Igiene Trop.* (Sez. Eritrea.) Asmara. 1942. Vol. 1. No. 2. pp. 105–106. English summary (2 lines).

Bellamy (R. Edward). **Observations on the Macroscopic Species-Identification of Larval *Anopheles* in Georgia.**—*Jl. Parasitology.* 1942. Aug. Vol. 28. No. 4. pp. 299–310.

When making surveys of breeding places of Anopheles it is useful to be able to recognize the various species in the field with the naked eye, even if such preliminary identifications are not entirely reliable. The author has found that in Georgia the fourth-instar larvae of *Anopheles quadrimaculatus*, *A. crucians*, and to a lesser extent *A. punctipennis*, can be distinguished with fair accuracy without magnification. In a test on over one thousand larvae there was an error of less than 4 per cent. The characters used for this purpose are set out fully in tables; these characters, however, are not mutually exclusive, they are merely relative. The author therefore concludes that they cannot be regarded as a reliable substitute for the usual microscopic identifications based on larval chaetotaxy. Their chief value lies in the help they give in recognizing the "microhabitats" of particular species within a given breeding place. *V. B. Wigglesworth.*

Frohne (W. C.). **Reconnaissance of Anopheline Larval Habitats and Characteristic Desmids of the Okefenokee Swamp, Georgia.**—*Public Health Rep.* 1942. Aug. 14. Vol. 57. No. 33. pp. 1209–1217. [15 refs.]

The Okefenokee Swamp occupies an area of some 700 square miles; the inhabitants are free of malaria though the disease is common in surrounding regions.

Very careful collecting of adult and larval Anopheles has shown that *A. crucians* is common and that it enters houses. Other species seem to be absent, including *A. quadrimaculatus*, which is very widely distributed and is the main vector of malaria in south-eastern United States.

The water of the swamp is very acid (*p*H 3·7 to 3·9 in general) and sphagnum moss is abundant. The author's personal interest appears to be in desmids (a group of microscopic Algae): he shows that they are particularly abundant in this type of water and gives a list of species characteristic of this swamp.

[The absence of most species of Anopheles from water containing sphagnum is evidently a widespread phenomenon, familiar in many parts of northern and central Europe. See also this *Bulletin*, 1940, Vol. 37, p. 181.] *P. A. Buxton.*

Smith (J. Vincent). **Outbreak of Malaria in a Cruiser at War.**—*Jl. Roy. Nav. Med. Serv.* 1942. July. Vol. 28. No. 3. pp. 234–244.

"During late April and early May 1941 the personnel of a cruiser, some 620 officers and men, were nightly subjected to the attacks of anopheline mosquitoes at the height of a malaria season." This paper describes the results of that nightly ordeal—159 cases of malaria, two of them fatal. [For obvious reasons, the locality of this sad experience is not disclosed, but references to climatic conditions then prevailing

afford some clue. From the symptoms described and other considerations one would have expected *P. falciparum* infections to have been predominant, but we are told that "benign tertian, quartan and subtertian infections were encountered and the first attacks were probably mixtures of at least two out of the three." The account gives a very graphic picture of the extreme difficulties of handling such an epidemic on board a cruiser on active service in war conditions. Experience taught the author that it is dangerous to withhold specific treatment until the diagnosis has been confirmed microscopically; all will agree. No parasites were found in the blood films of early cases; the staining of films in ships in tropical climes is said to be more difficult than ashore. The author considers that the modern idea of discarding quinine as a prophylactic is correct; he made no use of it. [Not many will subscribe to that modern idea. Most medical men with experience of malaria would certainly recommend the prophylactic use of atebrin or quinine by men for whom it was impossible to provide protection from mosquitoes "at the height of a malaria season," unless the stocks of these remedies were only sufficient for treatment of clinical attacks. Certain other views expressed by the author are unusual; the presence of crescents in the blood is not commonly regarded as an indication for giving quinine intravenously. On the other hand, had circumstances permitted the use of intravenous injections of quinine in certain of the cases described, some of the anxieties might have been avoided. Very many difficulties were surmounted in coping with this outbreak, and in the circumstances it is gratifying that there were not many more cases and more deaths.] *Norman White.*

Javett (S. N.) & Sacks (S.). **Chronic Meningococcal Septicaemia Simulating Malaria.** *South African Med. J.* 1942. Aug. 22. Vol. 16. No. 16. pp. 307-308. With 1 chart.

This is a report of an unusual and interesting case. An askari aged 23 fell ill in Tanganyika; he had high fever, generalized body pains, headache, chills, sweats and increasing weakness. The temperature rose every second or third day, sometimes two days in succession, in the late afternoon, to 102° or 103°. The paroxysms were always accompanied by sweating. The blood was not examined; a clinical diagnosis of malaria was made and the patient received 30 grains of quinine a day for 10 days. The symptoms continued. He was transferred to Kenya and four weeks later was admitted to a general hospital there. The temperature had assumed a definite tertian periodicity. Neither spleen nor liver was palpable. There was no rash. No parasites of any kind could be found in the blood. There was a polymorphonuclear leucocytosis. Arthralgia and myalgia persisted between the attacks. Quinine treatment was continued.

On the eighth day in hospital, after 35 days of intermittent fever, the temperature fell to normal. A five-day course of atebrin was given. The patient's general condition improved but he complained increasingly of headache. On the 42nd day of illness the patient had a rigor. Signs and symptoms of meningitis developed. Cloudy fluid withdrawn by lumbar puncture contained numerous pus cells and meningococci. Treatment with sulphapyridine effected a cure. There seems to be little doubt that this was a case of chronic meningococcal septicaemia.

[See also this *Bulletin*, 1942, Vol. 39, p. 738.] *Norman White.*

KILHAM (Lawrence). **Meningococcal Septicaemia with a Malarial Type of Fever.**—*Brit. Med. Jl.* 1942. Dec. 12. p. 696. With 1 chart.

This case closely resembles that described by Priest [this *Bulletin*, 1942, Vol. 39, p. 738]. There was a similar tertian or quartan periodicity of fever, the temperature falling to normal between paroxysms, and erythema nodosum; leucocytosis ranged from 12,000 to 17,000 during febrile periods, falling to 10,000 or less in the intervals. In the present case *N. meningitidis*, Group 2, was isolated twice from the blood of the patient (which was negative for malaria parasites) taken just before peaks of temperature. Rigidity of the neck and splenomegaly were absent throughout.

Before the diagnosis was established the patient was given sodium salicylate, and after that no further rise of temperature occurred, but a course of sulphadiazine was administered later, to lessen any chance of relapse. "This case illustrates the bizarre picture which may be presented in meningococcal septicaemia." *C. W.*

PERENCZI (Alexander). Klinische Beobachtungen ueber Malaria. [**Clinical Observations on Malaria.**]—*Deut. Med. Woch.* 1942. June 12. Vol. 68. No. 24. pp. 614–615.

Malaria is rare in Komarom and out of about 6,500 hospital patients only one case of the disease in 1939 and three in 1940 were reported, whereas in 1941 up to the end of October, 27 cases were seen. Twenty of these men, whose illness started between the end of April and the middle of July when mosquitoes were absent, had served during the previous autumn in endemic areas of malaria in the Siebenbürgen district, on the border of Hungary and Rumania. The author finds what he calls an incubation period of more than half a year strange, but makes no mention whether the men were receiving suppressive treatment during their period of exposure to infection, nor does he state the species of parasite found. Seven of the patients showed atypical clinical symptoms, and the only lesson to be learnt from the paper is the necessity for thinking of malaria when fever arises in patients who have previously been in malarious areas. *F. Murgatroyd.*

PUCCIARELLI (Amedeo). I gruppi sanguigni nella malaria. [**Blood Groups in Malaria.**]—*Riv. di Malariologia.* Sez. I. 1941. Nov.–Dec. Vol. 20. No. 6. pp. 353–365. [42 refs.] French summary (6 lines).

This paper starts with a discussion of the views of many authors regarding immunity to malaria, without reference, however, to a great deal of the most important work that has been done on the subject. This is followed by a discussion of work that has been published on blood grouping with special reference to the susceptibility of individuals of different groups to infections of varying kinds. The author's own observations relate to 160 cases of malaria. Of 73 persons infected with *P. falciparum*, 32 were Group A; 28 Group B; 7 Group AB; and 6 Group O. Of 26 *P. vivax* infections, 15 concerned Group A; 3 Group B; 3 Group AB, and 5 Group O. The only *P. malariae* infection was of a Group B patient. It is acknowledged that these observations as they stand have but little significance.

Norman White.

GUARDASCIONE (Vincenzo). Un raro caso di rottura spontanea della milza in soggetto malarico. [**Rare Case of Spontaneous Rupture of the Spleen in a Malarial Subject.**]—*Riv. di Malariologia.* Sez. I. 1941. Nov.–Dec. Vol. 20. No. 6. pp. 378–387. German summary (5 lines). [56 refs.]

A man aged 30 was treated for an acute attack of malaria with large doses of quinine. The spleen was palpable two finger-breadths below the costal margin. Three days after the return of the temperature to normal, when the patient appeared to be making satisfactory progress, the spleen ruptured and death quickly ensued. The post-mortem findings are described. The case serves as the text for a long interesting discussion on spontaneous rupture of the spleen, with very numerous references to the literature. *Norman White.*

FAIN (A.) & BENTZ. Observations sur des accès d'hémoglobinurie survenus dans deux consultations de nourrissons chez des jeunes enfants après administration de quinine prophylactique. [**Haemoglobinuria in Young Children attending Two Infant Welfare Clinics after Administration of Prophylactic Quinine.**]—*Ann. Soc. Belge de Méd. Trop.* 1940. Sept. 30. Vol. 20. No. 3. pp. 273–276.

The prophylactic distribution of quinine to native infants and young children has been practised for several years in the Lufimi-Lower-Sele region of the Belgian Congo. Quinine dihydrochloride in solution, 0·015 gm. per kgm. body weight, is given once a week. No harmful effects were ever noted till the occurrences reported in this paper. A child of three years received 0·2 gm. of quinine : some hours later it had a violent febrile attack and passed brownish-red urine. It was brought back to the Dumi Dispensary in the evening in a state of coma and died half an hour later. Six months later a child aged four years, from the same house as the previous case but of a different mother, was brought to the dispensary, the day following the administration of quinine, with a temperature of 39°C., prostration, vomiting, jaundice, and reddish-brown urine. It recovered. Four other cases of children, all aged about four years, are reported, from three other dispensaries in the district, in which the administration of prophylactic quinine was followed by the passing of red urine. Malaria is hyperendemic in the neighbourhood ; from 80 to 90 per cent. of young children are infected, mostly with *P. falciparum.* *Norman White.*

RAFFAELE (G.) & SANDICCHI (G.). Alcuni esperimenti con il prodotto sintetico Gamefar. [**Experiments with the Synthetic Preparation Gamefar.**]—*Riv. di. Malariologia.* Sez. I. 1941. Nov.–Dec. Vol. 20. No. 6. pp. 366–377. German summary.

Gamefar appears to be almost if not quite identical with plasmoquine. It is an Italian synthetic product manufactured by the S.A. Farmaceutici Italia, which also produces Italchina, the Italian atebrin substitute. Experiments are described which are exactly comparable with many that have been published with regard to plasmoquine. Nine *P. falciparum* gametocyte carriers, of whom two were patients undergoing malaria therapy and the remainder suffering from naturally acquired infections, each received 0·03 gm. of Gamefar daily for five successive days. The gametocytes were not very numerous in any of these cases. Their number increased in a few cases in the early days of

treatment but at the end of 10 days or less no gametocytes were to be found. From four of the patients Anopheles were infected before treatment was begun; attempts to infect Anopheles on the second day of treatment and later all failed. A supplementary experiment on three patients, all harbouring large numbers of crescents, showed that a single dose of 0·02 gm. of Gamefar was sufficient to destroy the infectivity of the blood for Anopheles. *Norman White.*

Ahmed (N.). **Five Years of Anti-Malaria Work at Lillooah Railway Settlement.**—*Jl. Indian Med. Assoc.* 1942. Aug. Vol. 11. No. 11. pp. 348–351. With 5 graphs.

Lillooah, about five miles to the north-west of Calcutta, is in the water-logged plain on the west bank of the Hoogly. It contains an important railway settlement. In 1933 *A. ludlowi* was found breeding in a tank. Malaria was very prevalent. There were about 600 tanks within a half-mile radius of the settlement, all of them prolific breeding places for mosquitoes. An energetic malaria campaign was started, in which filling, draining, oiling and Paris green were all utilized. The results have been gratifying. Days lost by a staff of 900, on account of malaria and "fevers," numbered 904 in 1938–39, as compared with 3,979 in 1934–35. Twelve species of Anopheles have been found in Lillooah; vector species were *A. philippinensis*, *A. culicifacies*, *A. varuna*, and *A. ludlowi*. *Norman White.*

d'Amato (Hugo J.). Profilaxia del paludismo en la República Argentina. [**Control of Malaria in Argentina.**]—*Bol. Oficina Sanitaria Panamericana.* 1942. Mar. Vol. 21. No. 3. pp. 233–235. English summary.

"During 1940 and especially from January to April, a decided increase in the number of cases of malaria was observed in the North Argentine region where the disease is endemic, with the exception of those areas protected by public health services, thus proving the efficiency of the methods applied. More than 170,000 patients were examined by the services of the National Department of Health and more than 20,000 in the provincial and municipal institutions (5% more than last year).

P. falciparum accounted for 33% of the infections as compared to 12% for the year before. Control work is on the dual basis of treatment and prevention. In 1940, 11,200 more patients were treated than in 1939, and more dispensaries were opened. Around 1,600 kg. of quinine are distributed every year. Health education is carried out intensively. Around 350,000 pesos are appropriated every year for preventive work, and private donations add about 50,000 pesos. In 1940, 30,250 houses were visited, in 8,210 of which mosquitoes were found, chiefly *Anopheles pseudopunctipennis*, and also a few *A. tarsimaculatus*, *A. argyritarsis*, *A. perizi*, and *A. albitarsis*. Drainage, filling-in, and other sanitary procedures were carried out on a large scale. More than 200,000 liters of petroleum and 70,000 kilos of Paris green were used. Studies are being made on improving malaria control methods, and the bio-chemical factors of larva breeding (in Salta, the influence of water and soil phosphorus)."

GUINDY: REPORT OF THE KING INSTITUTE FOR THE PERIOD FROM 1ST OCTOBER 1940 TO 30TH SEPTEMBER 1941. pp. 29–34.—**Studies on** *Plasmodium gallinaceum* [MENON (K. P.), AYYAR (P. V. Sitarama) & SHORTT (H. E.)].

In this report are given the results of various experiments with *Plasmodium gallinaceum*.

1. It is shown that the naturally occurring malarial parasite of the jungle fowl (*Gallus sonneratii*) is inoculable to chickens and is indistinguishable from *P. gallinaceum*. It is concluded that the jungle fowl is the natural host of this parasite.

2. It has previously been reported that exoerythrocytic schizonts could be demonstrated in chicks on the sixth day of the incubation period after inoculation of sporozoites. It is now stated that such forms have been found on the fifth day.

3. It is shown that the brain of a chick removed on the fourth day of the incubation period after sporozoite inoculation is infective to other chicks and that the brains of such brain-inoculated chicks are also infective on the fourth day. It is thus possible to make serial passages of the incubation period stages in the brains of chicks on the fourth day of incubation and similar results were obtained on the fifth and sixth days of incubation. The earliest day on which erythrocytic stages can be seen in the blood is the seventh day, but the blood is infective on the sixth day. [See also ADLER and TCHERNOMORETZ, this *Bulletin*, 1942, Vol. 39, p. 524.]

4. The effect of deep and superficial X-rays on sporozoites was studied as follows:—

(*a*) Sporozoites in *Aëdes aegypti* were unaffected by one hour's exposure. The mosquitoes still transmitted the infection.

(*b*) The exposure for an hour of the site of the injection of sporozoites in the chick did not prevent infection.

(*c*) Exposure for 7½ to 12½ minutes of citrated infected blood did not reduce its infectivity.

(*d*) The exposure of the site of inoculated blood did not prevent infection.

(*e*) Exposure of *A. aegypti*, before feeding them on infected chicks, did not prevent their infection.

[For the effect of ultra-violet radiation on sporozoites of *P. gallinaceum*, see this *Bulletin*, 1942, Vol. 39, p. 300.]

5. A volume of infected blood, mixed with an equal volume of 1 in 50,000 solution of methylene blue, lost its infectivity when exposed to bright sunlight for five minutes. There was no loss of infectivity without exposure to sunlight nor did blood lose its infectivity when exposed to sunlight in the absence of methylene blue. Gentian violet in the same dilutions showed no such photodynamic action.

6. (*a*) The blood of sporozoite-infected chicks is infective from the sixth day, while parasites are first seen in the blood on the seventh day.

(*b*) Sporozoites were still infective after 1½ hours in 0·85 per cent. normal saline or 2 per cent. citrated saline. After two hours they ceased to be infective.

(*c*) Sporozoites were injected into the pectoral muscle of chicks. The inoculated area was excised in one case after 18 hours, and in another after 24 hours. An emulsion of the excised tissue was not infective, suggesting the early removal of sporozoites from the site inoculated as the excision did not prevent infection of the original chicks.

(*d*) Massive doses of sporozoites dropped on to the scarified skin of two chicks failed to cause infection.

(*e*) Single infected red blood corpuscles injected into chicks failed to produce infection.

(*f*) It was not possible to infect geckos and toads by the injection of infected chick blood. *C. M. Wenyon.*

Missiroli (A.). Ueber die Entwicklung der Sporozoiten der Malariaparasiten. [**Development of Sporozoites of the Malaria Parasites.**] —*Zent. f. Bakt.* I. Abt. Orig. 1942. Mar. 26. Vol. 148. No. 7/8. pp. 359–363. With 1 fig.

This is a controversial paper in which the author argues against the findings of Kikuth and Mudrow, maintaining that these investigators have mistaken ordinary developmental forms of the bird malarial parasite, which may undergo schizogony in cells other than red blood corpuscles, for the immediate developmental forms derived from sporozoites. He again states that the early development of sporozoites takes place extracellularly in the lymph spaces of the tissues and not within histiocytes. [See also this *Bulletin*, 1940, Vol. 37, p. 671, and 1942, Vol. 39, p. 123.] *C. M. Wenyon.*

Porter (Richard J.). **The Tissue Distribution of Exoerythrocytic Schizonts in Sporozoite-Induced Infections with** *Plasmodium cathemerium*. —*Jl. Infect. Dis.* 1942. July Aug. Vol. 71. No. 1. pp. 1–17. With 2 text figs. & 8 coloured figs. on 1 plate. [31 refs.]

The authors have made a careful examination of the blood and organs of canaries infected with various strains of *Plasmodium cathemerium* and *P. relictum* with the object of determining the distribution in the body of exoerythrocytic schizonts. In a number of the strains it was not possible to discover any such forms, but in two of them they appeared when infection was produced by sporozoite instead of blood inoculation. In the case of birds inoculated with sporozoites it was found that in the early stages of the infection exoerythrocytic schizonts occurred only in the liver, spleen and bone marrow. At later stages of infection they were abundant throughout the body in endothelium and capillaries, and locally, in large numbers, in intravascular accumulations of macrophages which occurred in all the organs. It is suggested that two processes may be involved. In the one the exoerythrocytic schizonts are developed directly from sporozoites and occur in the liver, spleen and bone marrow, in the other they are the result of the developmental merozoites produced by erythrocytic schizonts finding their way into endothelial cells of all tissues and organs. *C. M. Wenyon.*

Boyd (Geo. H.) & Gilkerson (Seth W.). **Influence of Conditions of Latency upon Merozoite Production and Gametocyte Survival in** *Plasmodium cathemerium* **Infections of Canaries.** —*Amer. Jl. Hyg.* 1942. July. Vol. 36. No. 1. pp. 1–5.

The authors have studied the reproducing forms of *Plasmodium cathemerium* after inoculation of large numbers of parasites, taken from canaries at the height of an infection, into canaries which have had no

previous infection, and into canaries which have passed into the latent phase of infection. They have found that the schizonts appearing in the previously uninfected birds produce on an average 14 merozoites, while those in the previously infected birds give rise on an average to only 10·8 merozoites. It thus appears that there is some condition existing in the bird with latent infection which hinders multiplication, in that the schizonts produce a reduced number of merozoites. It has already been shown by BOYD that in any individual infection the schizonts are largest at the commencement of the infection and that they decrease in size and produce few merozoites as the crisis is approached. An increase in size occurs when the parasites are reduced in number at the crisis, but the size of the initial schizonts is never reached. In the case of gametocytes inoculated into previously uninfected birds and into birds with latent infection it was proved that they disappeared more rapidly from the blood of the former.

C. M. Wenyon.

HEWITT (Redginal). **Studies on the Host-Parasite Relationships of Untreated Infections with *Plasmodium lophurae* in Ducks.**—*Amer. Jl. Hyg.* 1942. July. Vol. 36. No. 1 pp. 6–42. With 10 figs. & 2 coloured plates. [26 refs.]

In 1938 COGGESHALL discovered a malarial parasite *Plasmodium lophurae* in a Borneo pheasant and successfully inoculated it to domestic fowls. It was maintained by inoculation of fowls or pheasants till WOLFSON in 1940 demonstrated its infectivity to ducks, in which, after intravenous inoculation of infected blood, the intensity of the infection far exceeds that produced by any other bird malarial parasite with the exception of *P. gallinaceum* in chickens. Interest in this parasite has increased owing to its suitability from the point of view of the size and convenience of the duck for experimental studies on malarial parasites. It was evident that if the duck was to be employed for such observations as complete a study as possible of the natural course of *P. lophurae* infection in these birds of various ages should be made. This the author of the paper under review has very largely accomplished and he gives a very full account of the results he has obtained. Special attention is paid to the influence of dose of parasites and the age and weight of the birds, on the resulting infections and the mortality rate. In order to observe the effect of infection on the blood it became necessary to study the normal blood picture of the duck, and the results of this study are fully described with the aid of a coloured plate illustrating the various blood cells encountered. Periodicity studies have been carried out and it has been shown that the degree of synchronicity is low, though it was possible to demonstrate that the asexual cycle occupied 36 hours. A coloured plate depicts *P. lophurae* at various stages of development in the duck. It is noted that so far it has not been possible to demonstrate for this parasite the exoerythrocytic forms which are such a prominent feature of *P. gallinaceum* infections in fowls. This, for certain chemotherapeutic experiments, is a distinct advantage.

The whole paper, which includes numerous tables and charts, is evidently the result of very careful study and observation. It will prove invaluable to all those who contemplate using ducks infected with *P. lophurae* for the study of malaria problems. *C. M. Wenyon.*

MARSHALL (E. K.), Jr., LITCHFIELD (J. T.), Jr. & WHITE (H. J.). **Sulfonamide Therapy of Malaria in Ducks.**—*Jl. Pharm. & Experim. Therap.* 1942. May. Vol. 75. No. 1. pp. 89–104. With 7 figs. [30 refs.]

In this paper the authors describe methods for testing possible antimalarial drugs on ducks infected with *Plasmodium lophurae*. In the first place the course of infection in ducks of a certain age and size was studied with a view to obtaining criteria for judging therapeutic activity. It was found that the highest percentage (about 85 per cent.) of red blood corpuscles was infected on the sixth day after intravenous inoculation of a standard dose of infected red blood corpuscles. By obtaining the percentage of infected red blood corpuscles in the blood on the sixth day it was possible to obtain a figure indicating the activity of a drug administered before this. This figure could be correlated with the survival time and the percentage survival. It was already found that for a satisfactory test it was necessary to keep the concentration of any drug in the blood as constant as possible. This could only be done by repeated daily doses. The procedure was finally adopted of incorporating the drug in any required concentration in the food and keeping the birds in alternating dark and light surroundings of three hours' duration. This procedure ensured that the drug was voluntarily ingested by the birds every three hours. By this method a large number of sulphonamide derivatives were tested and compared with quinine which, in the concentrations employed, reduced the percentage of red blood corpuscles infected on the sixth day from 85 to less than one. Of the sulphonamides tested, sulphapyrazine gave a figure of 2, *N'*methylsulphanilamide, sulphanilylguanidine, sulphathiazole and sulphadiazine a figure of five. Others gave higher figures and were thus less active as anti-malarials. It was of interest to note that *p*-aminobenzoic acid, itself having some antimalarial activity when administered alone, nevertheless had an antagonistic action on sulphonamides when given together with them.

This paper, which describes in detail the technique employed and the method of handling and feeding the ducks, and discusses the observations which led to the adoption of the standard method of testing drugs, is a most important one which should be carefully studied by all those working on the chemotherapy of malaria. *C. M. Wenyon.*

MARSHALL (E. K.), Jr. **Chemotherapy of Avian Malaria.**—*Physiol. Rev.* 1942. Apr. Vol. 22. No. 2. pp. 190–204. [108 refs.]

This paper is a review of literature—over 100 references are given—dealing with all aspects of the chemotherapy of avian malaria. It mentions the various species of bird malarial parasites which have been used for chemotherapeutic studies and the many drugs which have been investigated, including quinine and other cinchona alkaloids, atebrin, plasmoquine and the sulphonamides. Various special aspects of the subject are discussed. These include the action of drugs on different stages of the parasite, species and strain variation in susceptibility to drugs, the possibility of complete cure, drug-fastness, *in vitro* studies and the mechanism of action of drugs. A vast amount of information is contained in the 10 pages of the review, which should be read by all those who contemplate embarking on the chemotherapeutic investigation of bird malaria. *C. M. Wenyon.*

TRYPANOSOMIASIS.

DUREN (A.) & LEJEUNE (E.). Incidence de la trypanosomiase chez les Européens, fonctionnaires et agents du Congo Belge, de 1908 à 1939. Sa gravité et ses séquelles. La trypanosomiase maladie professionnelle. [**Trypanosomiasis in Government Officials in the Belgian Congo.**]—*Ann. Soc. Belge de Méd. Trop.* 1942. Mar. 31. Vol. 22. No. 1. pp. 1–9.

This review concerns 45 cases detailed in three tables. The general incidence among Government agents is approximately 0·75 per 1,000, but is 6–7 times higher among the medical personnel, and those engaged in itinerant service are twice as liable.

None of these patients is known definitely to have died of the disease, but enquiry was not complete at the date of publication.

C. C. Chesterman.

LAWSON (T. L.). **Trypanosomiasis treated with "Pentamidine."**—*Lancet.* 1942. Oct. 24. pp. 480–483.

This paper deals with the results of treating 53 cases of Gambian trypanosomiasis with diamidino diphenoxy pentane (pentamidine). The cases were not selected but were the first 53 diagnosed in the West Nile district of Uganda in 1941. The work was carried out under primitive conditions, but probably most of the cases had not been infected for longer than three or four months, since the entire population is examined for sleeping sickness once every three months. The chief clinical findings are recorded. After the clinical examination, enlarged cervical glands were punctured and the following blood examinations were performed: cell counts, estimation of haemoglobin and colour-index, differential white-cell count, and "separation of the blood" test. "For this test 8 c.cm. of blood is taken and diluted with 2 c.cm. of 3·8 per cent. sodium citrate (these proportions were chosen because a portion of the same blood serves for the sedimentation-rate). The mixture is left standing for 2 hours in a narrow test-tube. The plasma just above the level of the top of the sedimented cells is taken off, a film of the plasma made and stained with Leishman stain." Lumbar puncture was carried out; a cell count was done on the cerebrospinal fluid, which was also tested for excess of globulin by the Nonne-Apelt reaction with saturated ammonium sulphate; and finally, the cerebrospinal fluid was centrifuged and the deposit examined for trypanosomes. A thin blood film was also examined for parasites. It is interesting to note that in the 49 cases with positive gland puncture, trypanosomes were found on only two occasions in thin blood films. In the first 20 cases the blood was also examined by the triple centrifuge method, but although parasites had been found in the glands of all these cases, in only two were they found by this method.

Treatment with pentamidine was started after all these tests were completed, the drug being given daily by the intravenous route. Every day gland puncture was performed until the juice was negative for at least two consecutive days. After the third injection, all the investigations mentioned above were repeated. After the tenth injection, which completed the course for most of the patients, the investigations were again repeated. If a patient had a second course, the tests were done once more at the conclusion. Finally, all the cases were re-examined two to three months after the end of treatment.

As it was impossible to weigh the patients, dosage was regulated according to age. Patients between 6 and 10 were given 0·05 gm. at each injection ; patients of 11 and over were given 0·1 gm. at each. Of the 53 patients, 43 had 10 injections, 6 had 20 injections, one (a large man) had 10 injections of 0·1 gm. followed by 10 injections of 0·2 gm. ; one woman with a heavy infection had 3 injections of 0·1 gm. followed by 5 of 0·2 gm., but she was so weak after this that she was unable to get out of bed ; 2 patients had 6 injections, one receiving a total of 0·3 gm. and the other a total of 0·6 gm. All the injections were given daily by the intravenous route.

On examination two or three months after the end of treatment, 41 patients were clinically cured, three much improved, four improved and four unaltered or worse ; one had died. The results of examination of gland juice are as follows. Four cases were negative before, during and after treatment. Of the remaining 49 cases, which were positive before treatment, 31 had a negative gland juice after the first injection, 12 after the second injection, five after the third injection and one after the fourth injection. All these cases remained negative throughout the observation period. The state of the cerebrospinal fluid in the 53 cases before treatment is shown in the following table :—

Group	Cells per c.mm. CSF	Cases in group	Cases with excess glob.	Cases with trypanosomes +
1	Under 10	8	0	0
2	10–80	22	3	0
3	80–200	7	3	2
4	Over 200	16	16	5

As might be expected, the treatment had no significant effect on the cell count in cases of group 1, but 19 of the 22 cases in group 2 showed a reduction in cell count whilst under treatment. One patient refused further lumbar puncture, in one case lumbar puncture was not repeated owing to advanced pregnancy, and in one there was no alteration during treatment. Five of the seven cases in group 3 also showed a reduction in the cerebrospinal fluid cells during treatment. When they were re-examined two or three months after treatment, four of the seven cases showed an increase in cells above the original amount. In group 4, 14 of the 16 cases showed a reduced cell count on the completion of treatment. On re-examination at the end of two or three months, five showed a slight increase in the cell count and five an increase above the original count. One case in this group died after the course of treatment was completed.

The author states that it is interesting to note that in 12 cases the clinical findings and the results of cerebrospinal fluid examination disagreed. Of those treated, three had relapsed after having been treated with antrypol and tryparsamide two years previously. Two of these three cases showed no improvement, but the third improved remarkably in all respects. Details are given of a few of the more interesting cases.

Some toxic manifestations followed injection of the drug in 36 cases. These were increased pulse rate, feeling of heat all over the body, itching, nausea and vomiting, giddiness, and shivering. In a few

cases there was a slight fall in systolic blood pressure, and one patient had complete collapse resembling surgical shock ; he was almost pulseless for about a quarter of an hour, but recovered rapidly. All these symptoms lasted only a few minutes, and were less severe after successive injections.

The following are the conclusions :—

" The following facts are to the credit of pentamidine. It produces a rapid peripheral sterilisation of the blood and gland juice.

" Treatment is complete in 10 days instead of 10 weeks, as with other drugs available ; this is extremely important from the point of view of the patient and for the preventive medical aspect.

" Toxicity is low, especially in comparison with tryparsamide (which is responsible for many cases of blindness in Africa). The effective dose is not more than half the toxic dose and probably almost a fifth the lethal dose.

" On the debit side are its lack of success when the examination of the CSF shows serious CNS involvement. When the cell-count in the CSF is above 80 per c.mm., it is probably safer to use one of the pentavalent arsenicals. Some cases with counts above that figure were cured, but others were not.

" It is not safe to base too much reliance on the analysis of a mere 53 cases, but it does seem that this is probably the best drug so far produced for the early cases of sleeping sickness. If it is used, however, lumbar puncture should be done in all cases, and no case with a CSF cell count of 80 per c.mm. or more should be given pentamidine unless it can be carefully followed up. Control differential white-cell counts during treatment are advisable but not absolutely essential if dosage is reasonable. It is not practicable to give exact dosage per lb. of body-weight of the patient, since in Africa treatment is often in the hands of people who cannot calculate such niceties. Our rough method probably suffices in all but the most civilised surroundings."

[It is very doubtful whether some of these conclusions are entirely justifiable. There is no doubt that the diamidines produce rapid peripheral sterilization, as there is now abundant evidence on this point. There is, however, as yet little satisfactory evidence that the drugs are really of much use in patients with pronounced changes in the cerebrospinal fluid. Prolonged observation alone can decide this point, and it is to be hoped that the author will be able to extend his observation period far beyond two or three months.] *W. Yorke.*

Mazza (Salvador), Basso (Germinal) & Basso (Redento). Investigaciones sobre enfermedad de Chagas. Enfermedad de Chagas en primer período diagnosticada exclusivamente por biopsia de ganglio linfático con hallazgo de parásitos leishmaniformes. [**Early Diagnosis of Chagas's Disease by the Finding of Leishmania Forms in Lymphatic Glands.**]—*Universidad Buenos Aires : Misión de Estudiós de Patologia Regional Argentina Jujuy. Publicación No. 63.* 1942. 48 pp. With 49 figs.

Examination of sections of enlarged lymphatic glands, made from biopsy specimens, reveals leishmania forms of *T. cruzi*. This publication by Professor Mazza and his colleagues sets out an account of cases diagnosed in the early stages by these means and brings out the points with the wealth of detail that characterizes all articles associated with the name of the senior author.

Adenitis is associated with three stages of Chagas's disease: (1) Affection of the gland in anatomical connexion with the site of primary infection (inoculation chagoma); (2) Satellite lymphatic dissemination around the primary lesion (metastatic chagomata); (3) Generalization in viscera and the lymphatic system (haematogenous chagomata).

The authors describe the histological findings in four patients whose histories are given later, after the pathological description of the sections. The sections show, by the excellently reproduced photomicrographs, the condition of widespread histiocytosis, the cells containing leishmania forms of *T. cruzi*, often in large numbers. These histiocytes may be single or may fuse to form giant cells. In other parts of the sections may be seen infiltration by polymorphonuclear cells, swelling of the connective tissue, and some free leishmania forms of the parasite. Similar photomicrographs are given of all four cases whose histories and clinical course are related in the final section of the article. *H. Harold Scott.*

LEISHMANIASIS.

i. Swaminath (C. S.), Shortt (H. E.) & Anderson (L. A. P.). **Transmission of Indian Kala-Azar to Man by the Bites of *Phlebotomus argentipes*, Ann. and Brun.**—*Indian Jl. Med. Res.* 1942. July. Vol. 30. No. 3. pp. 473–477.

ii. Indian Journal of Medical Research. 1942. July. Vol. 30. No. 3. pp. 479–480.—**The Transmission of Kala-Azar.**

i. The experiments described in this paper, resulting in the infection with *Leishmania donovani* of five volunteers upon whom infected sandflies were allowed to feed, brings to a successful conclusion a series of investigations on the transmission of kala azar which were commenced in India 25 years ago.

In the first place the sandfly *Phlebotomus argentipes* was brought under suspicion on the ground that its distribution corresponded with that of kala azar. This was followed by the demonstration that leishmania ingested by the sandfly developed into flagellates which multiplied in the stomach and in many cases extended forwards to the pharynx, buccal cavity and mouth parts. With such flies a few transmissions of infection to animals by bite were effected, but positive results were so seldom obtained in the animals, while they completely failed in human beings, that it was felt that some essential factor must be missing. Finally it was discovered that if after the infective feed the sandflies were nourished on raisins instead of on blood, as had been the custom hitherto, there was a much greater development of flagellates, with the result that in a considerable percentage of the flies there occurred a complete blockage of the pharynx with the multiplying organisms. With flies infected and maintained by this technique a new series of transmission experiments to animals was instituted, with the result that transmission of kala azar by the bite of infected sandflies was successful in the case of the majority of the mice and hamsters employed [see this *Bulletin*, 1941, Vol. 38, p. 256; 1942, Vol. 39, pp. 447–449].

These successes encouraged further attempts to transmit kala azar to human beings. In a locality where kala azar does not occur, five healthy volunteers who had never left the district were selected, and on each were fed a number of sandflies which, after their infective feed on a case of kala azar, had been maintained on the raisin diet. The paper describes the infection of three of the five volunteers within a period of five to six months after the bites of the first batch of flies. In a footnote it is stated that since the paper was sent to press the remaining two volunteers had also been found to be infected.

The reasons for the past failures and the present successes are briefly discussed and it is suggested that two factors may have contributed to the positive results now obtained. The first of these is the effect of nourishing the flies on raisins instead of on blood, and the second a possible greater virulence of the parasites involved in the final experiments.

ii. The second paper is an Editorial Note in which are outlined the various stages in the investigation into the transmission of kala azar since its initiation in 1921 and the part played by the various investigators who were from time to time members of the Kala Azar Commission. A similar and more lengthy statement appeared in the *Indian Medical Gazette* (1942, August, p. 483). Both of these articles are of considerable value, for they have been written by those who are familiar with the work of the Commission from its commencement and are thus authentic records of the progress of the research, the discoveries which led to the final solution of the problem of transmission, and the names of those who were concerned with its elucidation.

C. M. Wenyon.

CHUNG (Huei-Lan.) **Localized Leishmaniasis of the Lymph Glands. With a Note by** V. T. LIEU.—*Chinese Med. Jl.* 1942. Jan.–Feb. Vol. 61. No. 1. pp. 19–25. With 8 figs. on 2 plates.

The case reported is that of a student in Peiping who complained of a small tumour in the mastoid region behind the left ear. It had been increasing in size for about a year when advice was sought. The tumour was excised, and when examined was found to harbour leishmania. The student was then admitted to hospital and a thorough examination for kala azar made. It was not possible to demonstrate leishmania by liver or sternal puncture or by culture. He was discharged from hospital and kept under observation till readmission to hospital nearly two years later suffering from pharyngitis and cough with slight temperature. The inguinal and epitrochlear glands were enlarged, as they were at the time of the first admission to hospital. On this occasion a lymph node from the epitrochlear region was removed. Leishmania could not be detected in sections or smears but a hamster inoculated with an emulsion of part of the gland became infected. A further examination failed to reveal leishmania in any part of the body. A third admission to hospital was made a year and a half later and no new developments were found except for continued enlargement of glands (post-auricular, submaxillary, cervical, epitrochlear, inguinal and hilar). Treatment with neostibosan was instituted. The conclusion reached is that owing to a good resistance the leishmania were localized in the regional lymph nodes and a visceral infection was prevented. *C. M. Wenyon.*

Chung (Huei-Lan) & Chow (Hua-K'ang). **A New Sodium Salt of Mannite Antimonic Acid in the Treatment of Kala-Azar in Chinese Hamsters.**—*Chinese Med. Jl.* 1942. Mar.–Apr. Vol. 61. No. 2. pp. 73–76.

The sodium salt of mannite antimonic acid, containing 21 per cent. of antimony, is supplied by the manufacturers (Merck, Shanghai) in 30 and 50 per cent. solutions in 2 cc. and 5 cc. ampoules. It is relatively thermostable and can be sterilized at a temperature of 100°C. without risk of decomposition. The solution can be injected intravenously, intramuscularly or subcutaneously. According to the manufacturers, white mice, rabbits and dogs can tolerate intravenous injection of 0·3 cc., 20 cc. and 40 cc. respectively of the 50 per cent. solution. The drug has been found effective against trypanosomiasis in white mice, but the experiments reported in this paper are the first to be carried out with this drug in leishmaniasis. These were conducted on experimentally infected Chinese hamsters. It was found that the drug had a low toxicity and high curative value. In fact, over three times the quantity of antimony can be administered in the form of this drug than can be given in solustibosan. With injections given twice daily a cure rate of $83{\cdot}3 \pm 15{\cdot}2$ per cent. was obtained. This cure rate in experimental kala azar has never been achieved with any other antimony compound.

If given to hamsters in toxic doses it gives rise to a diffuse vacuolar degeneration of the liver parenchyma and renal tubules, which is hydropic and not fatty in character. *C. M. Wenyon.*

Chung (Huei-Lan), Wang (C. W.) & Lee (C. U.). **Solustibosan in the Treatment of Kala-Azar.**—*Chinese Med. Jl.* 1942. Mar.–Apr. Vol. 61. No. 2. pp. 77–82.

The authors report the treatment of six cases of kala azar in Peiping with solustibosan administered either intramuscularly or intravenously. Generally 6 to 12 cc. were administered on alternate days, the total amount given varying from 60 to 162 cc. It is evident from the results obtained that the drug is as effective as ureastibamine or neostibosan, but in terms of the antimony content the amount required to produce a cure is much larger. Of the 24 patients 22 were cures, one was resistant and one failed to complete the course of treatment. The drug is a colourless solution containing 20 mgm. of metallic antimony per cc. Put up in ampoules it is stable, is of low toxicity and ready for administration either intramuscularly or intravenously.

C. M. Wenyon.

Cole (A. C. E.). **Cutaneous Leishmaniasis in East Africa.**—*East African Med. Jl.* 1942. Sept. Vol. 19. No. 6. pp. 199–200.

The author reports that several cases of kala azar, apparently contracted in the region north of Lake Rudolph, near the Omo river, Abyssinia, were admitted to a hospital in East Africa. Over half of the patients died, but of nine who recovered five developed a papular, nodular rash on the body, most marked on the face. The nodules coalesced to form a warty mass on the face and " a sort of reptilian

skin on the body, but the vegetation finally fell off or shrivelled up and regressed." All the papules contained leishmania; no special treatment appeared to be necessary.

A case of cutaneous leishmaniasis of the nose is also described from Kenya; it followed a slight abrasion. *C. W.*

FULLER (H. S.) & GEIMAN (Q. M.). **South American Cutaneous Leishmaniasis in Experimental Animals.** [Research Notes.]—*Jl. Parasitology.* 1942. Oct. Vol. 28. No. 5. pp. 429–431.

The authors give an account of their attempts to discover a suitable experimental animal for the study of *Leishmania brasiliensis*, the parasite of S. American muco-cutaneous leishmaniasis. The most successful result was obtained with the Texas ground-squirrel, *Citellus tridecemlineatus*. A number of these animals received subcutaneous injection of culture material. In each case after 21 to 44 days there developed a nodule at the site of injection. The nodule subsequently ulcerated and in some of the animals persisted for over 11 months. Leishmania were demonstrated in the lesions which consisted mainly of large mononuclear cells containing parasites. A number of other animals were inoculated and infections were obtained in some cases. In no case was intraperitoneal injection followed by a generalized infection. *C. M. Wenyon.*

FEVERS OF THE TYPHUS GROUP AND OTHER FEVERS.

FELIX (A.). **The Typhus Group of Fevers. Classification, Laboratory Diagnosis, Prophylactic Inoculation, and Specific Serum Treatment.**—*Brit. Med. Jl.* 1942. Nov. 21. pp. 597–601. [62 refs.]

This important report is of great interest to workers on the typhus fevers. The author begins by stating that the "typhus group of fevers" is now firmly established and that it comprises a number of different fevers in many parts of the world, some of which had long been known as "unclassed fevers." The recent recognition of these fevers as members of the typhus group is mainly due to the application of serological and immunological methods of study, especially the Weil-Felix reaction.

The author maintains that the original classification of these fevers suggested by the reviewer in 1921 and based on the arthropod vectors, although a step in the right direction, no longer holds good. "A satisfactory classification of the typhus group can be based solely on the antigenic type of the corresponding rickettsiae, upon which immunity and immunity reactions depend. The antigenic analysis of the various typhus rickettsiae has, however, not yet passed its infancy." Apart from *Rickettsia prowazeki* which has a heat-stable and alkali-stable antigen in common with *Proteus OX19*, the antigenic structure of the other Rickettsiae and their relationships to each other have not yet been studied, but with the discovery of yolk-sac and animal-lung methods of growing the organisms this gap in our knowledge will probably be filled very soon.

The classification proposed by the author is shown in the Table:—

TABLE I.—*Provisional Classification of the Typhus Group of Fevers.*

	Immunological Subgroup		
	Type OX 19	Type OX K	Type undetermined
ame of disease	Classical epidemic typhus Tabardillo (Mexico) Brill's disease (U.S.A.) Endemic typhus of U.S.A. and Australia, Greece, Syria, Manchuria, Malay (shop typhus), India, Burma, Philippines, Hawaii, Toulon, (fièvre nautique), etc.	Tsutugamushi fever of Japan, Formosa, Malay, and Dutch East Indies Scrub typhus of Malay, Dutch East Indies, India, French Indo-China, Australia	Spotted fever of Rocky Mountains Spotted fever of eastern U.S.A. São Paulo typhus Fièvre boutonneuse (Mediterranean) Fièvre exanthématique of Marseilles Febbre errutiva (Italy) Tick-bite fever of South Africa Epidemic and endemic typhus of South Africa Tick-borne typhus of India, Kenya, etc.
ector	Lice and rat fleas	Mites	Ticks, lice, and rat fleas
eservoir of virus	Rats. Man	Field mice and rats	Rodents. Dogs. ? Ticks. Man
gglutination ...	OX 19 +++ OX 2 + OX K —	OX 19 — OX 2 — OX K +++	OX 19 + OX 2 + OX K +

As has been shown by the author, a remarkably close relationship exists between the cross-immunity and agglutination reactions of the three *Proteus* strains, *OX19*, *OX2* and *OXK*. There are two well-defined serological types of disease (the *OX19* and the *OXK*) but the third "undetermined" group probably comprises several different types whose relationship to each other must await investigation, with the aid of pure cultures of the causal Rickettsiae, to determine the characters of their heat-labile as well as their heat-stable antigens.

The author's comments on nomenclature are timely: he criticizes the tendency to use different names for the same disease; for example the name "exanthematic typhus" is not suitable for louse-borne typhus because all the typhus fevers are exanthematic. [He might have added that some South American workers have recently applied the name exanthematic typhus to a variety of tick-borne typhus fever.]

The rest of the paper deals specially with louse-borne typhus. For laboratory diagnosis the only method of practical importance is the Weil-Felix reaction, which gives the most constant indication of louse-borne typhus. Rickettsia-agglutination and complement-fixation reactions have not yet been found practicable: reports on the results are conflicting. The various simple modifications of the Weil-Felix test are mentioned with approval; these have already been described in this *Bulletin*.

Immunity to typhus is very incompletely understood ; experiments on animals give only partial information. *R. prowazeki* has a heat-stable antigen which corresponds to the *O* antigen of *Proteus X19* in giving rise to the same agglutination and complement-fixation reactions, but it does not stimulate opsonin formation. CASTAÑEDA has shown that *R. prowazeki* has also a heat-labile antigen which gives rise to the formation of opsonins protective against infection by the same organism. This second antigen probably corresponds to the labile, somatic or *Vi* antigen of the typhoid bacillus which alone effectively immunizes animals against the virulent *Vi*+*O*-bacilli. The *O* antigen of *R. prowazeki* can be assumed to act as an endotoxin in the same way as the *O* antigen of the typhoid bacillus ; on the other hand the heat-labile antigen is not merely toxic, it has also the property of inhibiting the interaction between the *O* antigen and the *O* antibodies and thus protects the Rickettsiae from the opsonizing and bactericidal action of the natural and immune *O* antibody.

Attempts at chemotherapy have hitherto been unsuccessful ; in fact French workers with great experience of louse-borne typhus regard sulphapyridine as positively harmful. There is no convincing evidence that human convalescent serum or animal sera have curative value ; presumably because no sera yet obtained have both of the antibodies that result from the response to the heat-labile as well as the heat-stable antigens. In convalescent serum which cannot be obtained till two or three weeks after the end of the fever the *O* antibodies have already become greatly diminished, as is shown by the fall in the *OX19* titre. The same thing happens in the case of sera from hyperimmunized animals ; even in the early stages of immunization the *OX19* titre is low and it tends to fall during the period of rise in the titre of the neutralizing antibody.

The author suggests that this difficulty may possibly be overcome by immunizing animals with the alkali-stable *O* antigen of *Pr. OX19*, which is believed to be common to *R. prowazeki* and *Pr. OX19*. In collaboration with Dr. G. F. PETRIE he is at present engaged in immunizing horses on these lines and in three out of four animals the Weil-Felix titres have risen to between 1–20,000 and 1–60,000. It is hoped that clinical trials of this type of serum in combination with anti-Rickettsial serum will be made. Tests cannot be carried out satisfactorily on experimental animals because these do not show toxic symptoms comparable with those seen in typhus patients.

A typhus vaccine of maximum prophylactic value cannot be obtained till a number of important problems have been solved : we do not know the best means of maintaining the labile antigen in Rickettsial cultures or the best methods of killing and preserving the vaccine. Both phenol and formalin damage the labile *Vi* antigen of typhoid vaccine and the same thing may happen in the case of Rickettsial vaccines.

Vaccines are ordinarily tested either by finding the immunizing response in guineapigs or by estimating the *OX19* and neutralizing antibodies in the sera of inoculated persons. All three tests ought to be employed.

Tests of the *OX19* agglutination response in volunteers recently inoculated with various vaccines have been carried out. The results are shown in the Table. A rise in the *OX19* titre by 100 per cent. has been regarded as a "significant" increase in the antibody content.

ABLE III.—*Showing the OX19 Agglutinin Response in Volunteers Inoculated with Various Typhus Vaccines.* (*November* 1941 *to March* 1942.)

Vaccines			Number Inoculated	Number and Percentage showing Significant Rise in *OX 19* Agglutinin Titre	
Batch	Prepared from Rickettsiae grown in	Prepared or Issued		No.	Percent.
A	Yolk sac. European louse-borne strain	October 1940	68	3	4·4
B	,, ,,	May 10, 1941	144	25	17·3
C	,, ,,	November 4, 1941	125	62	49·6
D	Mouse lung. Tunisian louse-borne strain. (Dr. G. M. Findlay)	November 1, 1941	16	3	18·7
E	Rat lung. American murine strain	Date of expiry, April 1943	12	0	0

It will be seen that striking differences occur in the *O*-antibody response in these volunteers, whereas all the rabbits inoculated intravenously with the same vaccines responded with *OX19*-antibody formation.

Neutralization tests of the sera of the persons protected by the various vaccines are in contemplation.

In future it is likely that opsonin estimations will be employed to measure the response to the labile Rickettsial antigen, because, according to Castañeda, the *O* antibody plays no part in the production of antibodies for *R. prowazeki*.

Weigl's louse vaccine and the Rocky Mountain spotted fever vaccine made from infected ticks have already given encouraging results, but it is expected that vaccines made from Rickettsiae grown on animal tissues will prove equally effective.

[The existence of a "typhus group of fevers" was first suggested by the reviewer in a little-known article in the *Indian Medical Gazette* dated January 1917. The words used were:—"There are seven described diseases which may be included in the typhus group of fevers and which have much in common with each other. These are, Brill's disease, Rocky Mountain Fever, McNaught's South-African fever, MacKechnie's Kumaon fever, with which my own case may safely be grouped, the macular fever of Tunisia, and typhus fever." This and the later suggestion in 1921 that the fevers could provisionally be classified according to the arthropod vectors were made on purely clinical and epidemiological grounds at a time when no facilities were available in India for the Weil-Felix or other serological tests. A classification based on antigenic type will undoubtedly be adopted for the causal Rickettsiae but this will not necessarily be most suitable for the diseases as clinical entities. The classification of the diseases according to the vectors is being adopted to a steadily increasing degree and the author himself tacitly approves of the use of the vector's name in the nomenclature by calling classical typhus "louse-borne typhus." It is to be hoped that when the time is ripe for establishing a final nomenclature and classification the point of view of the clinician will be taken into account.] *John W. D. Megaw.*

BURNET (F. M.). **The Rickettsial Diseases in Australia.**—*Med. Jl. Australia.* 1942. Aug. 22. 29th Year. Vol. 2. No. 8. pp. 129–134.

This is an interesting lecture in memory of BANCROFT, who in 1876 discovered the adult worm *Wuchereria bancrofti*.

Rickettsial diseases are of minor importance in Australia, where, taken together, they probably kill less than 20 persons yearly. Classical typhus is now unknown. Flea-borne, endemic, typhus occurs in sporadic form, especially in Queensland, South Australia and West Australia. Unfortunately the one large outbreak at Toowoomba in 1926 was not completely investigated: there were 200 cases with only four deaths, and there was a plague of mice at the time. HONE in 1920 first described the disease in Adelaide and suggested that infection might have been derived from mice or rats.

Tsutsugamushi occurs in tropical Queensland. The author refers to the mysterious discovery of the *Proteus XK* strain which was originally brought from London to Kuala Lumpur by KINGSBURY: it was supposed to be a strain of *Pr. X19* but was found to be agglutinated by the sera of only those cases of typhus-like fever in which the reaction to *Pr. X19* was negative. These were later found to be cases of tsutsugamushi, to which the local names of scrub typhus and *XK* typhus were given. The mystery of the origin of the *XK* strain has never been solved; the discovery was a happy accident. In Queensland rats and bandicoots are the chief vertebrate reservoirs of infection; in Japan field mice. *Trombicula deliensis* is perhaps the only vector of mite-borne typhus; the author inclines to the view that the larval mites, which are believed to take only one blood feed, transmit the virus through their eggs to the larvae of the next generation, which then transmit infection.

Australia has no disease of the spotted fever group; the only tick-borne Rickettsial fever known in the country is "Q" fever, first recognized about eight years ago among workers in a slaughter-house in Brisbane. Cattle ticks are probably the vectors, but in abattoirs infection is believed to be acquired by inhalation of the dried faeces of infected ticks, or, possibly, through the skin. In nature the cycle is probably bandicoot—*Haemaphysalis humerosa*, but the scrub tick *Ixodes holocyclus*, with a wide range of hosts, probably forms the link between that cycle and abattoir infection. Fever and headache are the only prominent features, there is no rash, and infection does not spread from man to man. Bandicoots caught in the bush, and ticks from these animals, have been found to harbour the Rickettsiae. In Melbourne nine members of the laboratory staff have been infected with the disease; three of the attacks were moderately severe, the rest were sub-clinical. Infection is believed to have been caused by inhalation of infective dust which was probably liberated into the air while guineapigs' temperatures were being taken. *John W. D. Megaw.*

FANTA (Helmut) & SIEDEK (Hans). Ueber die Blutdruckverhältnisse im Gehirngefässgebiet bei Fleckfieber. [**The Blood Pressure in the Cerebral Arteries in Typhus Fever.**]—*Klin. Woch.* 1942. Oct. 3. Vol. 21. No. 40. pp. 881–883. With 1 chart.

The blood pressure in the cerebral arteries is the same as that in the retinal arteries and so could be estimated by the method of

H. K. Müller. A table shows representative findings in 11 patients who were in a state of stupor at the time of examination and in six patients whose mental condition was clear. The range of the readings (in mm. Hg.) was as follows:—

	Day of disease	Brachial artery		Retinal artery		Pulse
		Systolic	Diastolic	Systolic	Diastolic	
11 stuporose patients	6th to 10th	88–130	55–80	46–65	30–47	100–119
6 mentally clear patients	2nd to 12th	92–155	68–95	56–71	30–41	86–120
Normal readings for the retinal arteries				70–75	40	

Of the 11 stuporose patients eight gave systolic readings of 55 mm. or less; of the six mentally clear patients only one had a systolic reading of less than 66 mm.

The brachial blood pressure was surprisingly little affected; the systolic reading was less than 100 in only three of the stuporose patients and it was 112 or over in five of the six mentally clear patients. The maintenance of the systemic blood pressure at these relatively high levels was believed to be due to the free use of cardio-vascular tonics which included strophanthin, "cardiazol" [leptazol] and "sympatol." These drugs admittedly obscured the picture, but the authors do not believe that they were in any way responsible for the low pressures in the cerebral arteries, especially as these low pressures were still found in some convalescents in whom cerebral symptoms persisted for a considerable time after the omission of the drugs.

There was a general degree of positive association between the severity of the cerebral manifestations and the degree of lowering of the retinal (and therefore cerebral) blood pressure. The damage to the brain could not be explained on purely mechanical grounds; toxic factors must have played an important part in its production.

In convalescence there was usually a definite rise in the brachial and retinal blood pressure, though the latter remained persistently low for weeks in the type of case already mentioned. Sometimes the brachial pressure became unduly high in convalescence, probably because of an excessive reactionary response on the part of the vegetative (sympathetic) nervous system as shown by the occurrence of tachycardia, exophthalmos, mydriasis, tremor of the eyelids, anginal pains, sleeplessness, etc.

[As in most of the other German reports on typhus fever, great emphasis is laid on the importance of cardio-vascular tonics in treatment; in fact the authors state that the interests of the patients completely precluded them from omitting these drugs for the purpose of finding the normal cerebral blood pressures in typhus fever. No controlled tests seem to have been made to find whether there is a sound foundation for the firm belief in the efficacy of these drugs which is almost universally held by German physicians.]

John W. D. Megaw.

MALY (G.). Die Bedeutung der Weil-Felixschen Reaktion beim Fleckfieber und die Behandlung desselben mit Rekonvaleszentenblut. [**The Significance of the Weil-Felix Reaction in Typhus Fever, and the Treatment of the Disease with Convalescent Blood.**—*Klin. Woch.* 1942. Oct. 24. Vol. 21. No. 43. pp. 943–947. With 2 figs.

The author claims that the Weil-Felix reaction serves as an index of the degree to which the protective mechanism of the body is mobilized against the virus of the disease: it is not directly related to the activity of the virus. He regards a titre of 1–100 as suggestive of typhus and one of 1–200 as diagnostic.

The course of the reaction was closely followed in 100 patients. In 96 per cent. of all the cases with classical symptoms the rise and fall of the titre conformed to a regular pattern. At the end of the first week the reaction was negative (*viz.*, the titre was less than 1–200) in 58 per cent. and positive in 42 per cent. At the end of the second week or early in the third week the titre reached its highest point, say 1–1,600, and often remained constant at this high level for about a week. Early in the fourth week, sometimes a little sooner, the titre fell to a lower level, such as 1–400 to 1–800. Exceptionally, in the sixth week there was a second rise in the titre. From the 15th to the 18th week there was still a fluctuating positive ranging from 1–200 to 1–800.

Four exceptional cases were seen; in two of these the highest titres, 1–3,200 and 1–6,400 respectively, were reached in the fourth week: in the third case, which was severe, the titre remained constant at 1–800 from the third to the sixth week; and in the fourth case, an exceptionally mild one, the titre was 1–3,200 on the sixth day; 1–1,600 on the 12th day; 1–200 on the 19th day; 1–800 on the 25th, 28th and 30th days; thereafter it varied between 1–200 and 1–400.

Of the 100 patients, 60 had severe, and 40 had mild, attacks. The maximum titres are analysed in the following table:—

	Titres of 1–800 and under	Titres of 1–1,600 and over
Mild cases	11 (27·5 per cent.)	29 (72·5 per cent.)
Severe cases, treated with convalescent blood	11 (26 per cent.)	31 (74 per cent.)
Severe cases, not treated with convalescent blood	14 (78 per cent.)	4 (22 per cent.)

These findings are regarded as showing that the titre of the reaction is related to the intensity of the defensive reaction of the body rather than to the severity of the infection. In very mild cases the reaction may even be negative because there is only a slight demand on the defensive response; in very severe cases the reaction may also be negative because the defences are overwhelmed so that no antibodies are formed.

Examples are given in support of this view. It follows that in cases with severe symptoms a negative reaction or a low-titre agglutination is of bad omen. When death occurs in a case with a high-titre response there is probably a special localization of the lesions which leads to damage of a vital organ such as the brain or heart.

The relatively high titres observed in the cases treated with convalescent blood are regarded as being due to stimulation of antibody formation.

The importance of repeated tests at intervals of three days is stressed. In this connexion the various rapid tests are specially helpful because they can be carried out with one or two drops of blood obtained by pricking a finger or ear lobe. In doubtful cases the Rickettsia-agglutination test is useful when available. In negative cases histological examination of an excised " roseola " of the skin is diagnostic in the hands of an expert.

Convalescent blood was used in the treatment of 42 of the severest cases, in all of which recovery took place. The duration of the fever was not affected, but the temperature usually fell by lysis and there was often a prompt improvement in the general condition of the patients. The blood of the donor was taken at a period of high-titre response, usually about four days after the end of the fever. Preliminary tests for syphilis and relapsing fever were carried out. Each dose was 20 cc. of blood given by intramuscular injection and repeated once, twice, or three times at intervals of 24 hours.

In two cases intravenous transfusions of 100 cc. of convalescent blood were given with excellent results, but this method is attended with so many difficulties that it is impracticable except in well equipped hospitals.

The only drug mentioned with approval is adrenal cortical extract.

John W. D. Megaw.

VAN MEERENDONK (Piet). Erfahrungen ueber Fleckfieberbehandlung mit Atebrin und Calcium. (Vorläufige Mitteilung.) [**Experiences in the Treatment of Typhus Fever with Atebrin and Calcium.**]—*Deut. Militärarzt.* 1942. Sept. Vol. 7. No. 9. pp. 541–542.

The author claims to have demonstrated that a combination of atebrin and calcium is a specific treatment for typhus fever. He had already treated about 225 cases with atebrin alone, but although there was a reduction by about one-third in the case-mortality rate in persons aged 30 to 45 there were a good many cases with severe cerebral symptoms and several patients died after the end of the fever. In most of the fatal cases the post-mortem finding was encephalitis ; this and the occasional occurrence of a haemorrhagic rash indicated severe damage to the blood vessels, especially the capillaries. It was also noticed that the staining caused by atebrin was much more pronounced than in patients treated for malaria with the same doses of the drug. The author concluded that there must be a deficiency in the blood calcium, and this view was promptly confirmed by the results which followed administration of calcium. All the severest cases in the 20 to 40 age group [number not stated] treated with calcium responded with a prompt fall in the temperature, and none of them died. Severe cerebral symptoms and deafness ceased to occur ; the rash disappeared much earlier than in previous cases and never became haemorrhagic. Yellow staining also was much less.

Two examples are given of immediate response to the treatment. The calcium content of the blood in typhus patients was then estimated : it was found to be as low as 6 milligrammes per cent. It was also noted that patients treated with calcium never had the abnormally low blood pressures which are so striking a feature of the disease, and that cardiovascular tonics were seldom needed.

The association between calcium deficiency and circulatory disturbances is stated to be one of cause and effect. It was, therefore, concluded that whereas atebrin acts on the causal organism, calcium controls the organic changes occurring in the disease.

The treatment consists of one tablet of atebrin (0·1 gramme) thrice daily and at least 10 to 20 cc. of a 20 per cent. solution of calcium gluconate, or if this is not available, of a 10 per cent. solution of calcium chloride, once daily. In severe cases doses of as much as 40 cc. of one of these solutions were given daily. [Presumably by the intravenous route; the maximum B.P. dose of calcium chloride by this route is 1·0 gramme].

[In view of the reduction in the calcium content of the blood, treatment by calcium appears to have a rational basis. Neither this paper nor the previous one by the same author [see this *Bulletin*, 1942, Vol. 39, p. 679] contains evidence to justify the statement that atebrin acts on the causal organisms. There were no proper controls, we only have the author's opinion that the attacks would have been more severe but for the special treatment that was given.]

John W. D. Megaw.

STEINHAUS (Edward A.). **Rickettsia-like Organism from Normal *Dermacentor andersoni* Stiles.**—*Public Health Rep.* 1942. Sept. 11. Vol. 57. No. 37. pp. 1375–1377.

The ticks from which this Rickettsia has been recovered had for several generations been reared in the laboratory; in many feeding experiments they had never given rise to any disease in rabbits or guineapigs. The Rickettsia is most abundant in epithelial cells of the intestinal diverticula, but not in the nuclei. The organism is described; it has been established in fowl embryo culture, but has not grown on any of the large number of artificial media tried.

The Rickettsia occurs in the same species of tick as the morphologically similar Rickettsia of Rocky Mountain fever, but there is no cross immunity between the two, or between this Rickettsia and that of Q fever. The name *Rickettsia dermacentrophila* is suggested.

C. W.

BRIGHAM (George D.) & WATT (James). **Additional Highly Virulent Strains of Rocky Mountain Spotted Fever Virus isolated in Georgia.**—*Public Health Rep.* 1942. Sept. 4. Vol. 57. No. 36. pp. 1342–1344.

Most strains of the Rickettsia of Rocky Mountain fever isolated in the Eastern United States have been markedly less virulent for guineapigs than those commonly found in Montana, but there have been reports of the isolation of highly virulent strains in Washington [this *Bulletin*, 1940, Vol. 37, p. 843] and Georgia [*ibid.*, 1941, Vol. 38, p. 682]. The authors now report the isolation of four strains in Georgia, two from pools of *Dermacentor variabilis* taken from animals at a farm where a fatal case of Rocky Mountain fever had occurred, and two from the blood of two patients with the disease. Three of these strains were studied and compared with the previously isolated highly virulent strains. The scrotal reaction was constant in inoculated guineapigs; the fatality rate was high in these animals. By cross immunity tests the strains were proved to be identical with previously isolated strains, and typical lesions of Rocky Mountain fever were found in the brains of guineapigs.

In three human cases associated with these strains the Weil-Felix reaction with *Proteus OX19* test was positive in two (1 in 1,280 and 1 in 640 dilutions respectively) and negative in the third. *C. W.*

DE SILVA (Stanley). **A Ten-Day Fever simulating Typhoid.**—*Indian Med. Gaz.* 1942. Sept. Vol. 77. No. 9. pp. 532–533. With 1 chart.

Ten cases of pyrexia of unknown origin in Colombo are briefly reported. The onset was sudden, without chill; the temperature remained high for three to five days, then fell by gradual lysis. "The average duration of the fever was 10 days, the temperature invariably reaching normal on the tenth day." In one case the temperature rose to 101·8°F. for a few hours on the 23rd day. There was neither rash nor any other special feature. Agglutination tests for *Bact. typhosum*, *Bact. paratyphosum A*, *B*, and *C*, and for *B. columbiensis* [? *Bact. columbense*] were negative in every case. Clot cultures were made in five cases and stool cultures in four; all were negative. "The Weil-Felix test was done in two cases and proved negative" [presumably only *Proteus OX19* was used]. The average white blood count was 8,200, the lymphocytes were 40 per cent. Rapid recovery followed in every case.

[No epidemiological data are given except for the remark that the disease did not appear to be very infectious. These may possibly have been cases of one of the Rickettsial infections in which *Proteus OX19* is not agglutinated.] *John W. D. Megaw.*

PLAGUE.

MOLL (Arístides A.) & O'LEARY (Shirley). **Plague in the Americas. XI. Mexico.**—*Bol. Oficina Sanitaria Panamericana.* 1942. Sept. Vol. 21. No. 9. pp. 874–883. With 1 map & 1 chart. [Refs. in footnotes.]

XI. *Mexico.*—Mexico qualifies with the United States as the only two North American countries "known to have suffered an invasion of plague." The figures for Mexico are: a total of about 868 cases with 590 deaths in the two main periods 1902–3 and 1920–23. These are represented in some 17 foci radiating from the three seaports Mazatlan, Veracruz and Tampico. As usual, for the history of original plague invasion at a seaport, there is uncertainty about the mode of entry. Plague entered Mexico through Mazatlan in 1902, probably from San Francisco. The disease was at first thought to be a "rare and malignant form of malaria." Some 8,000 or 9,000 persons fled the city and the epidemic lasted from October 20th, 1902, to March 17th, 1903, when the last human case occurred. The total number of cases reported was 475, with 69 per cent. mortality. Plague appeared next officially in Veracruz on the other side of the country, but not till 1920, in which year also it was reported in Tampico. In this outbreak the last sporadic cases of human plague were recorded in 1923. Anti-plague campaigns were instituted and followed the usual lines:—compulsory notification; capture and destruction of rodents; isolation of cases; disinfestation and deratization; cyanide fumigation; quarantine and inspection of travellers; vaccination and serum therapy. Most of the cases were bubonic. In Tampico,

where 156 cases were studied, the percentages were: bubonic 84, septicaemic 13, pneumonic 2, and carbuncular 1, while the case mortality for the bubonic plague throughout the country was 63–77 per cent., which is rather high. *W. F. Harvey.*

SCHWARZ (Ernst). **Notes on Commensal Rats.**—*Amer. Jl. Trop. Med.* 1942. Sept. Vol. 22. No. 5. pp. 577–579.

The author points out that in American literature the rat usually referred to as *R. rattus alexandrinus* is in fact *R. rattus frugivorus*. The under side of *frugivorus* is white or lemon yellow sharply set off from the back; that of the true *alexandrinus* is grey, passing gradually to the brown of the back. Both of these exist in the United States.

R. r. rattus and *R. r. alexandrinus* are primarily house rats, but *R. r. frugivorus* tends to nest in trees; control measures usually taken are effective against *R. norvegicus*, *R. r. rattus* and *R. r. alexandrinus*, but may miss *R. r. frugivorus*.

In East Africa rats of the Nile valley, Lake Victoria, Lake Tanganyika and the Ituri forest regions are descended from *R. r. alexandrinus*; since the construction of the Uganda railway these rats have spread towards the coast. Rats of Indian origin have been carried inland from the coast, and *R. r. kandiyanus* (*wroughtoni*) has been found at Nakuru and Kisumu. It is known that in East and South Africa and in Egypt the wild rodents are infected with plague, but human plague in these areas is chiefly found where the commensal rats are infected; direct transmission from wild rodents to man is rare.

The paper ends with remarks on the importance of identification of ship rats and the aid this may give in the tracing of the origins of epidemics. *C. W.*

JORDAN (Karl). **On the Siphonaptera collected by Dr. J. M. de la Barrera in the Province of Mendoza during 1939.**—*Rev. Inst. Bacteriológ. "Dr. Carlos G. Malbran."* Buenos Aires. 1942. June. Vol. 10. No. 4. pp. 401–460. With 34 figs.

HENNESSEY (R. S. F.). **Pneumonic Plague.**—*East African Med. Jl.* 1942. Sept. Vol. 19. No. 6. pp. 183–190.

In the nine years since 1933 there have been 38 autopsies on patients dying of primary pneumonic plague. In 26 cases the condition was true lobar pneumonia, not confluent bronchopneumonia; in 11 of the remainder it was the classical haemorrhagic bronchopneumonia. It is necessary to emphasize this fact, lest the pathologist, taking the classical haemorrhagic bronchopneumonia of plague as his guide, decide against the diagnosis of *P. pestis* infection. Fulminating plague and virulent plague generally give rise to bronchopneumonia which at the time of death has scarcely passed the stage of red hepatization. We may assume, therefore, that in view of the occurrence of extensive and advanced lesions of the lobar type, the strains of *P. pestis* in circulation in the Kampala District of Uganda are of reduced virulence. Pneumonia is also a terminal event in bubonic and septicaemic plague. In that case the mechanism of production would seem to be either a pneumococcal bronchiolitis "followed by a secondary invasion of the damaged lung tissue by *Past. pestis via* the blood stream," or an embolic deposition of the organism in the lung tissue with extension to bronchi and a generalized bronchopneumonia. *W. F. Harvey.*

CHOLERA.

PANJA (G.). **A New Method of Isolation of Vibrios from Cholera Stool.**—*Indian Jl. Med. Res.* 1942. July. Vol. 30. No. 3. pp. 391–396. With 1 fig.

During a search for filter-passing vibrios in cholera stools it was found that vibrios would grow through an L3 candle into surrounding peptone water much earlier than such organisms as *Bact. alkaligenes*, motile coliform organisms and late lactose-fermenters. This finding has been put to practical use in the isolation of cholera vibrios and the procedure has been greatly improved by adding boric acid to the peptone water, which caused inhibition of growth of coliform organisms, but not of vibrios. The acid, in a strength of 0·08 per cent., was added to the peptone water and *p*H adjusted to 9. A small amount of the stool is mixed with the peptone-water and partly aspirated through the candle into the surrounding boric-peptone-water by vacuum action. A pure growth of vibrios was found in most of the samples after 18 to 20 hours' incubation. The candle must of course be tested for porosity and leakage before use. This method, which gave an 87 per cent. success as against 44 per cent. by direct bile-salt agar plating does not differentiate between Inaba or Ogawa subtypes or El Tor and non-cholera vibrios. A figure in illustration of the apparatus is given.

W. F. Harvey.

BACILLARY DYSENTERY.

PAULLEY (J. W.). **Treatment of Bacillary Dysentery in the Middle East.**—*Lancet.* 1942. Nov. 21. pp. 592–594.

BUTTLE, in experiments *in vitro*, failed to find any difference between the bacteriostatic effect of sulphaguanidine and sulphapyridine against dysentery organisms. In comparing the effects of treatment with these sulphonamides cases were drawn from an area of a few square miles in the Middle East over the period April to July 1942. Most were mild : a few moderate or severe.

They were divided into groups according to the treatment given :—

(1) Salines plus sulphaguanidine whenever necessary.
(2) Sulphaguanidine.
(3) Sulphapyridine.
(4) Kaolin.

All were seen and treated within one or two days of onset.

The patients all passed blood and mucus and were diagnosed on the exudate in the faeces, though the rate of isolation of dysentery bacilli was low. Most were Flexner ; a few Shiga, Schmitz and Sonne.

In 60 cases treated with salines supplemented later with sulphaguanidine, the average period in bed was 12·6 days. In 25 treated with sulphaguanidine only, the period was 5·36 days. In two groups of 43 and 30 treated with sulphapyridine it was 4·26 and 4·96 days ; in 15 with kaolin the average was 6·1 days. In an outbreak of severe Shiga dysentery the average periods in bed were 5·7 days in 15 treated

with sulphapyridine and 8·01 in 13 with sulphaguanidine. It is therefore concluded that treatment with sulphonamides proved superior to other methods, but that sulphapyridine possesses advantages over sulphaguanidine.

It is necessary that sulphonamide treatment should be initiated in the acute stage. When sulphaguanidine is scarce there is a good case for the use of sulphapyridine, though there is certainly more danger of agranulocytosis, and this necessitates making leucocyte counts if the drug is given for longer than 4–5 days. No patient in this series required sulphapyridine for a longer period than four days. The advantages of sulphonamide treatment in bacillary dysentery are the speed of recovery and the fact that solid food can be taken early and the patient does not require prolonged convalescence.

One patient developed haematuria after 2½ days of sulphapyridine. The drug was immediately discontinued, but the dysentery was cured. Haematuria cleared in three days on fluids plus massive alkali treatment by the mouth.

It was therefore decided to prescribe Pot. cit. grains 40 two hourly in the initial stages for all patients passing a large number of stools on admission. It is important that a daily urinary output of 1,500 cc. should be maintained and it is probable that a reaction of *p*H 11 is necessary before crystallization of sulphonamide can be averted with certainty. *P. Manson-Bahr.*

COLE (Seymour L.). **Sulfaguanidine Toxicity.**—*Jl. Amer. Med. Assoc.* 1942. Sept. 19. Vol. 120. No. 3. pp. 196–197.

The occurrence of severe reactions due to sulphaguanidine has not hitherto been recorded, but that the clinical use of this drug is not without hazard is shown by the following case. The diagnosis of ulcerative colitis was made in a woman, and treatment with sulphaguanidine was instituted ; the first dose was of 0·1 gm. per kgm. body weight, the succeeding doses were of half this amount, and were administered every four hours. On the ninth day, after having taken 110 gm., the patient complained of severe headache and nausea ; at this point the drug was discontinued.

The following day the patient's temperature, previously normal, was 104°F., and there was a diffuse morbilliform rash on the body and limbs ; the urine contained many crystals of sulphaguanidine and the blood contained 2 mgm. of sulphaguanidine in 100 cc. The patient "looked extremely toxic," and in spite of high fluid intake, secreted little urine. Under the continued regimen of forced fluids, however, the temperature fell in a few days to normal, and the rash disappeared.

It is regarded as possible that the drug was absorbed more rapidly through the ulcerated areas of the large intestine than would be the case with an intact mucous membrane, and this should be taken into consideration in determining the amount of sulphaguanidine to be administered to patients with ulcers in the gastro-intestinal mucosa.

C. W.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

Berkman (J. M.) & Bargen (J. A.). **Amebic Abscess of the Liver with Choledochal and External Fistulas : Report of Case.**—*Proc. Staff Meetings Mayo Clinic.* 1942. Sept. 9. Vol. 17. No. 31. pp. 481–487. With 1 fig.

The patient whose record is cited here is a physician of 42 years who apparently contracted amoebic dysentery in 1925 ; this was followed by a large, indolent rectal abscess, which was drained. In the meantime he had established the diagnosis by demonstration of *E. histolytica* in the faeces. Symptoms being controlled by emetine injections and stovarsol, he was believed to be cured, and a quiescent period of eight years ensued, during which he was free from obvious intestinal disturbance. The pyrexia, lassitude, night sweats and increasing pulmonary symptoms forced him to enter hospital, where, on account of a leucocytosis of 19,000, a retrocaecal appendix abscess was suspected and the appendix removed. During convalescence signs of liver abscess became apparent. The pyrexia yielded temporarily to heroic doses of emetine, but his condition remained unsatisfactory.

On admission to the Mayo Clinic in April 1941, he had slight pyrexia, but all routine laboratory tests were negative, except for increased blood sedimentation rate. The leucocyte count was well within normal limits. An exploratory laparotomy revealed a liver abscess in the lower aspect of the right lobe beneath the attachment of the suspensory ligament, which yielded 1200–1500 cc. of thick yellow pus ; *E. histolytica* was found in the exudate on the 13th day of drainage. Emetine hydrochloride 1 gr. was instilled into the sinus from time to time and usually caused a severe reaction. By October 1941 he had taken altogether 120 gr. (8 gm.) of emetine. In spite of intensive emetine therapy a further laparotomy was undertaken in January 1942. The abscess cavity contained more pus ; it was widely opened, drainage tubes were inserted and the cavity irrigated with 2 per cent. chiniofon (quinoxyl). No form of anti-amoebic treatment was subsequently given until April 1942, when it was noted that the drainage was bile tinged.

On injection of the sinus with opaque medium it was found that a direct connexion existed from the abscess cavity to the common bile duct and hence into the intestine. It was then decided to press anti-amoebic treatment regardless of risk. Finally, in July 1942, the sinus tract closed. More than 194 gr. (12·9 gm.) of emetine hydrochloride had been administered.

[This account illustrates the necessity of treating amoebic dysentery radically from the commencement.] *P. Manson-Bahr.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Robinson (G. G.). **The Relative Toxicity of Rotenone and Pyrethrum in Oil to the Argasid Tick, *Ornithodorus moubata*, Murray.**—*Bull. Entom. Res.* 1942. Dec. Vol. 33. Pt. 4. pp. 273–281. With 3 figs. [15 refs.]

In laboratory tests in which known amounts of rotenone in various media and Pyrethrum in a medium petroleum oil were sprayed under

standard conditions upon *Ornithodorus moubata* it was found that rotenone is far less toxic to this tick than an equal weight of pyrethrin I. The author concludes that Pyrethrum is therefore more economical to use than Derris as a contact insecticide for *Ornithodorus*. It has been difficult to find a suitable solvent for rotenone ; but it is here shown that it is highly soluble in cresols, xylenols and phenols, and that such solutions may then be diluted with mineral and vegetable oils. Rotenone does not deteriorate if stored in the dark in these mixtures. Medium petroleum oil leads to much more rapid penetration by the insecticide than vegetable oils such as ground-nut oil [*cf.* this *Bulletin*, 1942, Vol. 39, p. 847 ; 1943, Vol. 40, p. 89.] *V. B. Wigglesworth.*

Robinson (G. G.). **Fertility in the Argasid Tick, *Ornithodorus moubata*, Murray.**—*Parasitology*. 1942. Nov. Vol. 34. Nos. 3/4. pp. 308–314. [12 refs.]

Davis (Gordon E.). ***Ornithodoros parkeri* and Relapsing Fever Spirochetes in Southern Idaho.**—*Public Health Rep.* 1942. Oct. 2. Vol. 57. No. 40. pp. 1501–1503.

" In a relatively restricted area in southern Idaho there is a very heavy infestation of *Ornithodoros parkeri* in ground squirrel and prairie dog burrows and an unusually high incidence of spirochetes.

" Of a total of 1,466 ticks collected, 1,298 were tested in 163 sublots, 69 of which were positive for spirochetes.

" This is the heaviest infestation of *O. parkeri* thus far encountered in any one area in the nine States (Wyoming, Colorado, Utah, Montana, Washington, Oregon, Nevada, California, and Idaho) in which this species has been collected, with the possible exception of an isolated area in central California. The number of spirochete strains recovered far exceeds all others.

" Relapsing fever has not been reported from this area."

Das Gupta (B. M.). ***Spirillum minus* Infection Acquired from an Indian Squirrel (*Sciurus* sp.).**—*Indian Med. Gaz.* 1942. Sept. Vol. 77. No. 9. pp. 541–542. With 1 chart.

The record of a typical case of rat-bite fever in a boy 12 years old following a bite on the finger by an Indian Squirrel (*Sciurus* sp.).

The patient developed an attack of fever about two weeks later, but did not come under the author's observation until after about six weeks. Blood taken from the patient was then inoculated into two guineapigs and four young mice. One of the guineapigs and three of the mice became positive for *Spirillum minus* after unusually prolonged incubation periods (15 to 26 days). After one injection of 0·3 gm. novarsenobillon the patient's fever disappeared and a second dose of 0·45 gm. a week later prevented any relapse. *E. Hindle.*

LEPROSY.

SCHNEIDER (Kurt). Einiges ueber das Memeler Lepraheim und die Lepraendemie im Kreise Memel. [**Leprosy in the Memel Region.**]—*Deut. Med. Woch.* 1942. June 12. Vol. 68. No. 24. pp. 615–617.

The author deals with the prevalence of leprosy in the Memel region. The early history of infection through a Lithuanian servant girl in 1848 is referred to. The disease was still endemic in 1899, when a leper home was opened for the isolation of 16 patients, who, since 1893, had been isolated in cottages. In 1909 the beds were increased to 22, and later the number rose to 28; since 1920 no new cases have occurred. Details are given regarding five infected areas which are of local interest, but show that the disease largely died out leaving a few old cases still in the leper home. Recently these numbered seven; four from the Memel area, two Lithuanians, and one from Brazil. Isolation of the infective patients is enforced, but bacteriologically negative ones may be allowed to reside in hygienic houses. Various remedies have been tried, and chaulmoogra oil has some beneficial effect, but X-rays were found to be harmful. No benefits were observed from the use of vitamin B_1 in nerve cases. *L. Rogers.*

FERNANDEZ (Jose M. M.) & OLMOS CASTRO (Norberto). La reacción precoz provocada por la lepromina. Investigaciones efectuadas con diversos antigenos derivados del *Mycobacterium leprae.* [**The Early Lepromin Reaction. Study of Antigens obtained from** *Mycobacterium leprae.*]—*Rev. Argentina de Dermatosifilologia.* 1942. Vol. 26. Pt. 3. pp. 556–580. With 11 figs. [17 refs.] English summary.

This is a comprehensive and well-thought-out article dealing with several points, each of which might form the subject of a separate contribution. The authors write first of the early reaction following injection of whole lepromin in lepers, in those in contact with lepers, and in persons thought to be healthy. In this section they refer to previous work [see this *Bulletin*, 1940, Vol. 37, p. 632]; this will be referred to again later in this abstract. They then define their terminology and record the results in lepers, contacts and the healthy. They next give an account of their investigations into lepromin filtrate, the method of its preparation, characters of the reaction and the results of its use in the same three classes of subjects. Thirdly, they carried out analogous tests, using tuberculin and other antigens, and pass on to consider the work of LOWE and DHARMENDRA [this *Bulletin*, 1942, Vol. 39, pp. 227–228], and the sensitization of non-leprous persons with whole lepromin. Such is the general scheme of this article, and on each of these points more details must be given.

In a study of the intradermal injection of lepromin in 1940 the senior author showed by tests on 312 patients and 250 contacts that: (1) Twenty-four hours after injection, in positive cases, an erythematous infiltration showed itself, reaching its acme in 48 hours, beginning to decline in 72 hours and disappearing in a week, when the later, Mitsuda, reaction began. (2) Early and late reactions are both positive in 92 per cent. of cases of leprosy. (3) Use of a filtrate of whole lepromin

gives in certain cases the early reaction, but the later, nodular, reaction fails to appear. (4) This latter reaction is not a non-specific one because it is seen only in those who react to whole lepromin.

The authors define " whole lepromin " (lepromina integral) as the antigen which contains all the constituents of a leproma—bacteria, cells, tissue detritus. By " bacillary lepromin " they imply an antigen of a suspension of bacilli obtained by the method of MONTAÑES, or some similar process. " Purified lepromin proteins " are the soluble active substances of *Mycobacterium leprae*, obtained by filtration or chemical extraction, containing no acid-fast bacteria. The reactions produced are of two types, the early erythematous infiltration, mentioned above, and the later, papular or nodular, three or four weeks later. The following is a brief account of the authors' results with these various antigens tested on the different groups of subjects.

i. *Whole Lepromin.*

Early Reactions in Lepers and Contacts.—Their later investigations have confirmed the authors' previous findings, that a positive early reaction is never seen in a lepromatous case ; that in most allergic cases both reactions, early and late, occur and correspond in intensity ; that some do not give an early reponse, but show a moderate or weak late reaction ; and, lastly, they have never seen a case of early positive response with negative late reaction.

Early Reactions in Subjects believed to be Healthy.—Two hundred and fifty-seven children, from 3 to 15 years of age, in an orphanage, were inoculated with whole lepromin ; of these, five (1·9 per cent.) gave the early reaction and 98 (38·1 per cent.) the late, third week, reaction. Clinical examination of the five early reactors revealed in four of them a scar of the " residual tuberculoid type "—evidence of an old infection. Among 120 adults supposedly free from lepra infection, two gave the early reaction. Seventy-two of these were observed for the late reaction and 58 (80·5 per cent.) were positive.

ii. *Lepromin Filtrate.*

The mode of preparation of this is important and is given as follows : Nodules rich in bacilli are cut small, boiled for 30 minutes in water to remove the epidermis, then reduced to a paste by grinding in a mortar ; distilled water is added, 10 cc. for each gramme of the fresh nodule, and made into a smooth paste in a mortar and then filtered through gauze and the filtrate passed through a filter candle, L3. The filtrate from this is concentrated at 58°C. to one-tenth of the original suspension, so that 1 cc. represents 1 gm. of the nodule. It is then placed in ampoules and sterilized by heating in the autoclave for half an hour at 120°C. For injection 0·1 cc. is used.

The reaction begins to be visible within 24 hours and reaches a maximum in 48 hours as an erythema round the point of injection, 10–30 mm. in diameter, very like the Mantoux reaction. It then begins to fade and in a week is recognizable only as a dark pigmented spot.

Reaction in Lepers and Contacts.—In 50 patients with the lepromatous form the reaction was negative, as it was also with whole lepromin. Of 55 with the tuberculoid form 50 gave the early reaction, none the late reaction, whereas the same fifty gave the early response to whole lepromin and 53 the late reaction.

Of 25 contacts 18 gave an early (48 hours) response ; 18 gave the early response to whole lepromin and 21 the late.

Reaction in Supposed Healthy Subjects.—Of 103 of these one was positive with early response, whereas to whole lepromin one gave the early and 39 the late.

iii. *Early Reaction in Individuals Sensitized to* Mycobacterium tuberculosis *and other Antigens.*

The authors state that positive reactions occur in tuberculous persons not suffering from leprosy. The other antigens used were Frei's of lymphogranuloma inguinale and Dmelcos of soft chancre. The results were negative in all [but only eight of the former and two of the latter were tested].

The investigations of LOWE and DHARMENDRA are referred to and discussed, but these have already been abstracted in this *Bulletin* [1942, Vol. 39, p. 227].

iv. *The Sensitization of Non-Leprous Persons by Means of Whole Lepromin.*

On the hypothesis that the early reaction was due to previous sensitization by toxins or antigens of *Mycobacterium leprae*, the authors aimed at provoking sensitization of persons believed to be free from leprosy by intradermal inoculation of whole lepromin. One group of 15 healthy adult women were injected intradermally with whole lepromin and another with the filtrate. None gave the early reaction, but 13 gave the late reaction to the former (whole lepromin). Twenty-five days after the first injection lepromin filtrate was injected ; three gave a definite early response, two a doubtful or weak positive, ten were negative. In other words, an early reaction was obtained with the filtrate in three at least of the fifteen who had previously given a negative response to whole lepromin.

Using Dharmendra's protein antigen in 61 adults believed to be free from leprosy and who had never had injection of whole lepromin, 7 gave a frank positive and 3 others a weak positive reaction. Of another 37 adults, believed to be free from leprosy but who had had one or more injections of 0·1 cc. whole lepromin, Dharmendra's antigen produced positive reactions in 30, or four-fifths of the subjects. Five had had their injections of whole lepromin 3 years before and three of them were positive, two negative ; three had had it one year before, two were positive ; twenty-six had had it 2 months before and 23 were positive, and of three who had had the injection only one month before two were positive.

To epitomize, the authors state : " The results of the early reaction to whole or ' integral lepromin ' coincided in the great majority of cases (94 per cent.) with those of the late nodular reaction in lepers and contacts. Both reactions were negative in the lepromatous forms of the disease, frequently positive in the neural forms and more so in the tuberculoid variety. In healthy people both reactions frequently gave diverging results : the early reaction was usually negative (98·05 per cent.), while the Mitsuda reaction was frequently positive (38·13 per cent.). These persons could be sensitized by intradermal injection of a sufficiently active ' integral lepromin ' antigen and a large number of positive early reactions were then observed.

"A filtrate of 'integral lepromin' produced the same early reaction as integral lepromin in patients, contacts and healthy persons. This antigen did not produce a late nodular reaction. The antigen prepared according to Dharmendra's technique (soluble proteins of *Myco. leprae*) gave similar results to those obtained with the filtrate."

H. Harold Scott.

Dixon (H. B. F.). **Clinical Lecture on Leprosy : with Notes on Three Cases amongst Maltese Troops.**—*Jl. Roy. Army Med. Corps.* 1942. Sept. Vol. 79. No. 3. pp. 118–132. With 1 chart.

Fox (Howard). **A Case of Leprosy of Sixty-One Years' Duration.**—*Arch. Dermat. & Syph.* 1942. Oct. Vol. 46. No. 4. pp. 552–553. With 1 fig.

Ignacio Chala (José). Sulfuro de antimonio coloidal en la lepra. [**Colloidal Antimony Sulphide in Leprosy.**]—*Rev. Facul. de Med.* Bogotá. 1942. July. Vol. 11. No. 1. pp. 1–12. With 3 plates.

Salts of antimony, especially the tartrate, have been used in the treatment of the leprous reaction. The author here reports the results of using the isotonic colloidal sulphide, Stibicol, in treatment of the disease itself. Stibicol contains in each cc. 0·002 mgm. of antimony in the metallic state. It is given in doses of 2 cc. injected intramuscularly or deep subcutaneously every three days till 12–14 doses have been given. Then, after an interval of two weeks, another series is started. Tolerance was perfect ; there were no cases of colloidoclasic shock, but care was taken to exclude any nephritic patients from the treatment.

Three cases are described in detail. The first was a man of 22 years with tuberculoid leprosy and maculae on face, arms and legs and patches of hypoaesthesia on the limbs. Treatment was started on March 6th, 1941, and he had seven series of injections. On the 22nd July, 1941, the maculae had gone, except for slight pigmentation, and bacteriological examination was negative. When he was seen again a year later the improvement had been maintained. [It is a little difficult to reconcile the recorded points here. For a single course of 12–14 injections, one every three days, 5–6 weeks would be needed ; that is, with the two weeks' interval, 7–8 weeks before the second series of injections would be started. Seven courses would thus take 40 weeks or more. From March 6th to July 22nd is two days short of 20 weeks.]

The second case was in a man of 41 years, with rhinitis, maculae and infiltrations of face, forehead, neck, back, trunk, thighs and legs, and scattered patches of anaesthesia. He received six series of injections, starting on August 25th, 1941, and by May 1st, 1942, the rhinitis and maculae had disappeared and bacteriological examination of the nasal mucus and of gland smears was negative for Hansen's bacillus.

The third patient was a man of 40 years with scaly erythema and nodules of the face, neck, thorax and legs, and patchy analgesia. He was given three series of intramuscular injections, each of 2 cc., three times a week, with an interval of 20 days between the series. Seven months after beginning the treatment it was reported that the maculae had almost gone, the sensory changes were no longer present and "the infiltrations were obviously better."

[In spite of the extensive lesions in each case the patients seem to have come under treatment early, for the history states clearly that the first, aged 22, was 22 years old when the initial lesion presented itself; the second was 41 years of age and the first lesion was observed when he was 41 years 4 months old. The third, aged 40, noticed the initial lesion six months before. None of these patients had had any other treatment. "The number of injections in each case fluctuated between 65 and 90" [but the third can have had only 42 at the most, and perhaps only 36 according as his course was 14 or 12 injections]. [The method is worthy of further trial, but the discrepancies shown in this record lead one to doubt, and, anyway, no generalization can be based on so few cases.] *H. Harold Scott.*

HELMINTHIASIS.

Schwetz (J.) & Dartevelle (E.). Sur les mollusques gastéropodes pulmonés et la schistosomiase de l'Est du Kivu-Ituri et spécialement dans l'agglomération de Kasenyi au Lac Albert. [**On the Pulmonate Gasteropod Molluscs and Schistosomiasis of the Eastern Side of the Region between Lake Kivu and the River Ituri and especially in the Villages of the Kasenyi Region on Lake Albert.**]—*Ann. Soc. Belge de Méd. Trop.* 1942. June 30. Vol. 22. No. 2. pp. 123–156. With 2 maps & 3 figs. [11 refs.]

During the work of the malaria mission of the Belgian Royal Colonial Institute in 1939, Schwetz studied the molluscs of this region, and Dartevelle identified the species collected. They were not able to stay long in most of the districts studied; their stay in the Kasenyi region, where they worked for 10 days in October at the end of the dry season and before the rains, was their longest stay in any one place. van den Berghe studied the molluscs here for six weeks during June and July 1936; Becquaert is the only other worker who has studied them. Schwetz and Dartevelle regard their results as preliminary only and plead for an extended study lasting a year and including both wet and dry seasons.

The study is important because bilharzia is common all over the eastern border of the Belgian Congo, and especially at Irumu and Buna in the Upper Ituri region and in the region of the mines of Kilo and on the shores of the Bay of Bobandana (Lake Kivu). They studied the Kasenyi region more especially, but the distribution of the disease elsewhere needs investigation.

It has been thought that the fisheries in Lake Albert near Kasenyi are responsible for most of the cases, because fishermen are presumably in contact with water contaminated by the intermediate hosts of Schistosoma; but the lake fishing is done with nets in deep water, and little fishing occurs in the creeks, etc., along the lake shores, where the molluscs that probably transmit the disease abound [but see Scops, below]. Further, Schwetz and Dartevelle found that the miners of Kilo were at least as heavily infected with Schistosoma as the fisherfolk. Of the adult men examined at Kilo, who had nothing to do with water or the lake, 40 per cent. had *S. mansoni*; notably fewer of the women and adolescents were infected. Scops has shown that about 50 per cent. of the men and women workers alike in the

village were infected, and that the percentage in the fisherfolk is never higher than that of the other workers. Thus the fisheries are not the chief source of the disease. The main sources seem to be the rivers and creeks, where little fishing is done.

The rivers Kisegge, Ndiggi, Sabe and Mwita were investigated in the Kasenyi region. The River Kisegge resembled all the other rivers of this region in being dry in October when it was examined, except for collections of water still left after the dry season ; these were used by the natives as sources of drinking and washing water ; near the lake the river became marshy, with many aquatic plants and a small lagoon. The flat, sandy and muddy shores of Lake Albert in the Kasenyi region give place in the north to higher steep banks and to the south to marshy shores covered by vegetation and reeds. The bay of Kaseke is shallow and covered with aquatic plants and harbours many molluscs.

A list is given of the six species of Planorbis found between Lake Kivu in the south and the Upper Ituri and Lake Albert in the north. These are :—

P. choanomphalus and *P. stanleyi* in the semi-lacustrine focus at Bobandana (Lake Kivu).

P. adowensis at Irumu and in the Mongbwalu region (Upper Ituri).

P. boissyi tanganikanus, *P. choanomphalus*, *P.* (*Gyraulus*) *natalensis* and *Segmentina kanisaënsis* at the most important focus of the disease at Kasenyi (Lake Albert). The minute species *Gyraulus natalensis* predominated greatly over all the others.

A list is also given of the other gasteropods and of the Lamellibranchs found.

VAN DEN BERGHE, in the subsequent discussion, pointed out that Gyraulus and Segmentina are very abundant in the estuaries and near marshy banks of lakes and on the stalks of aquatic plants above the water, so that their ecology differs essentially from that of Planorbis ; he collected thousands in a few minutes on Lake Kisale in 1933 and at Kasenyi in 1936 ; they have never been proved capable of transmitting schistosomiasis ; he searched hundreds of them in vain for trematodes. He was able, however, to transmit *S. mansoni* to monkeys and mice by means of *P. adowensis*, which he found at Kasenyi in 1936.

Schwetz and Dartevelle think that all these species may transmit schistosomiasis, except the minute species of Gyraulus and Segmentina. They could not find cercariae in *Gyraulus natalensis* or *P. choanomphalus* in the brief time available, but they did find them in *P. adowensis* in the Mongbwalu region. Until the results of a prolonged study of the molluscs during both the dry and the wet seasons are available, the only prophylactic measure possible is treatment of the patients, although this will not prevent infection. *G. Lapage.*

SCOPS (Ch.). Note au sujet de la bilharziose dans la plaine de Kasenyi (Lac Albert). [**Note on Schistosomiasis in the Plain of Kasenyi (Lake Albert).**]—*Ann. Soc. Belge de Méd. Trop.* 1942. June 30. Vol. 22. No. 2. pp. 155–165.

In 1937 Scops examined 30,000 natives of the Gety-Bogoro-Boga plateau. The preliminary results of a second examination in 1938 showed that 65 per cent. of the people examined had intestinal

bilharziasis. In 1939 a further examination was made. Two tables show the very high incidence in the various localities investigated in August 1938, and in June 1939.

In 1938 the average percentage of people infected among those examined was: men 46 per cent. of 161 examined; women 27 per cent. of 148 examined; children 15 per cent. of 169 examined. In 1939 the corresponding figures were: men 34 per cent. of 979 examined; women 30 per cent. of 431 examined; children 10 per cent. of 609 examined. Out of 2,597 people examined, 690 (26 per cent.) were infected.

Not only the natives but also strangers, travellers and business men, especially those associated with the fisheries, were infected. The high incidence among children is explicable by their preference for aquatic games. The natives infect themselves by contact with the lake water, especially at the mouth of the River Semliki (between Lakes Edward and Albert), where they walk in the muddy, stagnant water to fish; or by washing in or drinking the water of the River Kisegge (Lake Albert) and its tributaries, which is used by all the natives for these purposes [*cf.* SCHWETZ and DARTEVELLE, above]. These are the two main sources of the infection in this area. Schwetz, during the subsequent discussion, said that he could not confirm this.

Prophylactic measures suggested are the treatment of the infected patients, prevention of fishing by them until they are cured, destruction of the molluscs of the River Kisegge, interdiction of all fishing at the mouth of the Semliki and the provision of a European doctor to investigate the whole problem.

A third table shows records of the number of natives in whom Ascaris, Trichuris, Taenia and ankylostomes were found in 1939. This shows that Ascaris is the next most frequent helminth after Schistosoma, both in children and adults. The highest incidences of it were 44 per cent. in men, 40·8 in women and 44 per cent. in children in different localities. The strange fact was that ankylostomiasis was very rare or absent, only one case being noted. During the subsequent discussion Schwetz agreed with this; but VAN DEN BERGHE pointed out that Scops had not used floatation methods, which are necessary to reveal hookworm eggs, although he thought that they do not reveal schistosome eggs so well as examination in water or saline. van den Berghe had found that 7 per cent. of examined persons were carriers of the eggs of *Necator americanus* at Kasenyi and 40 per cent. at Irumu, where the low nocturnal temperature kills the larvae in faecal cultures. By numerous autopsies done at Elisabethville in 1933 he had found, to his surprise, only a few specimens of *Necator americanus* in the duodenum, often less than 10. *G. Lapage.*

DAVIS (George Bertram). **Observations on the Facial Appearance in Cases of Bilharziasis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1942. Aug. 31. Vol. 36. No. 2. pp. 117–120. With 4 figs. & 1 diagram.

Young natives not under five years old and not over 14 show very often a facial appearance characteristic of bilharzia, namely loss of subcutaneous fat definitely localized in the region of the horizontal ramus of the mandible. This makes the outline of the face, when it is seen from the front, run straight down to a point in front of the angle of the lower jaw and from there straight to the chin, or with a slight

convexity upwards between the angle of the lower jaw and the chin, owing to the indrawing of the tissues round the middle of the lower jaw. The result is a triangular appearance of the lower half of the face instead of the evenly rounded contour of this part of the normal face. The author's photographs illustrate this well.

This bilharzia face can be a useful aid to diagnosis, but it cannot be relied upon by itself. Using it during the examination of natives in kraal schools (in Rhodesia) the author found that, in one series of 133 children between 5 and 14, correct diagnosis was indicated by the bilharzia face in 83·4 per cent., *i.e.* 94 showed the bilharzia face and had eggs in the urine, and 12 showed the normal face and had no eggs in the urine. In another series of 1,006, in which the age of the patients was not taken into account, 67 per cent. showed correct results (bilharzia face with eggs in the urine in 622 cases, no bilharzia face and no eggs in the urine in 52 cases).

Many subjects showing no bilharzia face with eggs in the urine were below the age of four years or over 14. In a child under four years wasting of the chubby face is difficult to see and at the age of 15 the face is beginning to lose its fat.

It is possible that, in cases with bilharzia face and no eggs in the urine, further examination would have shown the presence of eggs, or that these cases had been treated and the face had not had time to recover, or that the infection was at its earliest stage when the bilharzia face is very difficult to detect.

The author's investigation revealed 90 per cent. of cases of bilharzia in 2,000 natives examined in Southern Rhodesia (Metemwa).

G. Lapage.

BRAUNE (Johann-Friedrich). Ueber die Verhütung der Bilharziose unter Feldzugsbedingungen, insbesondere ueber die Gewinnung von zerkarienfreiem Wasch- und Badewasser. [**On the Prevention of Schistosomiasis under Campaigning Conditions, especially on the Provision of Washing and Bathing Water Free from Cercariae.**] *Deut. Trop. Ztschr.* 1942. Aug. 15. Vol. 46. No. 16. pp. 409–426. [14 refs.]

In areas where bilharzia exists all water should be regarded as dangerous; but in war only simple measures for rendering it safe, which need little transport and labour, can be applied. Prevention of the entry of the cercariae into the skin is then more important than killing the snails, prevention of the fouling of water by faeces and urine or treatment of personnel with antimonial preparations.

Two chlorine preparations, both available in powder or tablet form and both stable, were tried and both were shown to be effective. The two preparations were (1) Clorina, previously called Hydrosept, a chloramine preparation (p-toluolsulfonchloramide of sodium); its formula is given; it is very stable, easily soluble in water and contains about 25 per cent. of active chlorine; and (2) Caporit, which is calcium hypochlorite containing 70–75 per cent. of active chlorine. It is stable, can be kept dry for several months without marked loss of chlorine, and readily dissolves in water.

These were both tested in Hamburg tap water and in the dirty water of the Elbe against cercariae of *Schistosoma mansoni* obtained by experimental infestation of *Planorbis guadeloupensis* in the Hamburg Tropical Institute.

It made little difference whether tap water or Elbe water was used, although the cercariae died rather more quickly in the chlorinated Elbe water. Stirring helps the lethal action. All the experiments were done at 20–24°C.; at 29–30°C., which is nearer tropical temperatures, no significant difference in the times required to kill the cercariae was noticed.

Following the work of KLEPETARS, acid was added to quicken the action of Clorina. Citric and tartaric acids were used, experiment having shown that these did not, in the concentrations used, damage the cercariae. In practice hydrochloric or other cheaper acids could be used. Results with both citric and tartaric acids were the same.

Clorina, in a concentration of 1 gm. per 10 litres (the author calculates the capacity of a wash basin as 4–6 litres and a bucket as 10–12 litres) of Elbe or tap water, with the addition of 1 gm. of citric or tartaric acid, killed all the cercariae within 10 minutes. The same result followed when 0·5 gm. clorina, with 2 gm. citric or tartaric acid was used; but the former is better because it uses less solid material and gives the added safety of a chlorine content twice as high. If the acid is left out a substantially longer time is required (0·5 gm. Clorina in 10 litres then required 125 minutes).

Caporit has a higher chlorine content and worked as well in weaker solutions, 1 gm. of Caporit freeing 100–200 litres of tap or Elbe water within 10 minutes and 200–500 litres within 15 minutes. Its action did not begin to fall off until the sixth day. It requires no acid. It is thus more useful for larger quantities of water. A tablet of 0·1 gm. is enough for a bucket or basin.

All the experiments were done in glass vessels and probably apply to basins, baths and other containers with solid walls, but collections of water in the open were not tested; in these vegetation, bacteria and organic matter would probably reduce the action of the chlorine.

Neither Clorina nor Caporit in relatively strong solutions (1 gm. Clorina and 1 gm. citric acid in 10 litres of water or 1 gm. Caporit alone in 100 litres) could kill *Bulinus contortus*, the intermediate host of *S. haematobium*, or an unidentified species of Planorbis after 18 hours.

The Seitz filter layers in the German Army Knapsack Filter cannot be penetrated by cercariae. In 108 litres of water pumped through this filter after three litres of water heavily contaminated with cercariae had been pumped through it, no cercariae were found. The dangers of infection when using the filter or when cleaning it are pointed out.

The concentration of both Clorina and Caporit which will kill cercariae will also kill the bacteria in drinking water. *G. Lapage.*

MAZZOTTI (Luis). La cuti-reacción y la intradermo-reacción aplicadas en un caso humano de *Fasciola hepatica*. [**Cutaneous and Intracutaneous Tests in** *F. hepatica* **Infection.**]—*Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1942. Mar. Vol. 3. No. 1. pp. 53–55. English summary.

"Cutaneous and intracutaneous tests in a patient infected with *Fasciola hepatica*, gave positive results.

"Intracutaneous tests using the same antigen were negative in six patients with onchocerciasis and one patient infected with *Taenia saginata*." [The antigen was an extract of *F. hepatica*.]

CHEN (H. T.). **The Metacercaria and Adult of *Centrocestus formosanus* (Nishigori, 1924), with Notes on the Natural Infection of Rats and Cats with *C. armatus* (Tanabe, 1922).**—*Jl. Parasitology.* 1942. Aug. Vol. 28. No. 4. pp. 285–298. With 12 figs. on 1 plate. [19 refs.]

The author worked on material collected in the Kowloon area of Hong Kong. He briefly outlines the history of the genus Centrocestus and describes the metacercaria in detail. Earlier descriptions of it have been brief. The metacercarial cysts occur most often attached to the gill filaments of four freshwater fish, *Macropodus opercularis*, *Puntius semifasciolatus*, *Carassius auratus* and *Misgurnus anguillicaudatus*, but are also found in the stomach wall and muscles of a common frog, *Rana limnocharis* and of a common toad, *Bufo melanostictus*. A list of other fish hosts in Formosa, the Philippines and Hong Kong is given.

The adult was obtained experimentally in the small intestine of white rats, mice, rabbits, cats and dogs. To these hosts may be added *Nycticorax nycticorax* in Formosa and *Bubulcus ibis coromandus* and *Pyrreroides manilensis* in the Philippines, and in Hong Kong chickens and ducklings. Descriptions of the adult are available only in Japanese, but the author gives a full description, elucidating some obscure points.

The diagnosis of the three known species of *Centrocestus* (*C. armatus*, *C. formosanus*, *C. cuspidatus*) is discussed, the eggs being the most reliable feature for determining these. Existing data cannot decide the optimum normal definitive host. More adults were recovered by the author from rats than from the other hosts that he used, but this does not necessarily mean that rats are the optimum hosts. There is some evidence of acquired resistance to the parasite.

The discovery of the metacercariae of *C. formosanus* in frogs and toads shows that Heterophyid metacercariae, hitherto known only from fish, can infest other hosts also. This makes it necessary to revise the family Heterophyidae, Ohdner, 1914, and the subfamily Centrocestinae, Looss, 1899.

It may also have public health importance, provided that it can be shown that the metacercariae infest edible frogs, such as *Rana rugulosa*. The author "has good reason to believe" that *R. rugulosa* may be involved and is investigating the question further. The danger is the greater because frog meat is most delicious when it is cooked in a "lightning" manner. The only fish involved in this area so far are all small and are not used as food.

Centrocestus is transferable to man and may have been overlooked, because it is so small ($461 \times 212\ \mu$) and because its eggs resemble those of common human flukes, *e.g.*, *Clonorchis sinensis*. *G. Lapage.*

RICARDO BENAVENTE (Garces). Contribución al tratamiento de los quistes hidatidicos pulmonares con pneumotorax pre-operatorio (método de Arc). [**Treatment of Pulmonary Hydatid Cysts by Pre-operation Pneumothorax.**]—*Rev. Med. de Chile.* 1942. May. Vol. 70. No. 5. pp. 344–362. With 8 figs. [36 refs.]

HU (Stephen M. K.). **Studies on the Susceptibility of Shanghai Mosquitoes to Experimental Infection with *Microfilaria malayi* Brug. VII. *Culex fuscanus* Wiedemann.**—*Chinese Med. Jl.* 1942. Mar.–Apr. Vol. 61. No. 2. pp. 94–97.

"1. The susceptibility of *Culex fuscanus* to infection with *Microfilaria malayi* has been confirmed.

"2. Of 68 *Culex fuscanus* fed on two cases of *Microfilaria malayi* infection, 2 or 2·9 per cent. were found with mature filarial larvae in them.

"3. Fourteen of the mosquitoes were found with only dead encapsulated microfilarial form larvae, while the remaining 53 mosquitoes were negative for any filarial larva.

"4. *Culex fuscanus* is not likely to play a significant role in the transmission of *Microfilaria malayi* infection in the lower Yangtze region because in this part of the country it seldom enters houses or feeds on man."

DAMPF (Alfonso). La Carretera Panamericana y el problema de la oncocercosis. [**The Pan-American Highway and the Problem of Onchocerciasis.**]—*Bol. Oficina Sanitaria Panamericana.* 1942. Aug. Vol. 21. No. 8. pp. 753–758. With 1 map. English summary.

Among other problems that will arise from the construction of numerous means of communication over the American continent are medico-entomological ones. Remote places will be placed in contact with the advantages and disadvantages of civilization and diseases transmitted by insects that are confined to such districts will suddenly make contact with other populated areas, creating new foci and new problems.

A typical example is the construction of the Pan-American Highway crossing Mexico from Nuevo Laredo to Suchiate and passing through or near foci of onchocerciasis. This disease occurs in two Mexican States, Oaxaca and Chiapas; elsewhere in America it occurs only in Guatemala, its focus of origin. The author has shown that Simuliidae exist not only in the affected areas, but also in other parts of Mexico, especially along the rivers of the plateaux of the Gulf of Mexico and the Pacific. The spread of onchocerciasis is thus an international problem.

The map published shows the Pan-American Highway. The primary focus of onchocerciasis, in Oaxaca State, is so far from the Highway that it is no danger to travel; but the Highway virtually passes through two foci of the disease in the State of Chiapas; and this also happens in Guatemala. The Simuliidae occupy in all the four foci areas more extensive than those occupied by the disease; there is imminent danger of the extension of the disease not by the infected Simuliidae but by carriers of the microfilariae using the new means of communication.

None of the three known vectors of onchocerciasis (*Simulium ochraceum*, *S. callidum* and *S. metallicum*) has been found in the isthmus of Tehuantepec, and they are absent from the area between the Oaxaca focus and those in the States of Puebla and Veracruz. They have not been studied over those parts of the Highway which run to Matamoros in Puebla, to the interior of Oaxaca State or down from the Oaxaca plateau to the isthmus. Investigations are required of the Simuliidae of the western Sierre Madre Range of the States of Michoacan, Jalisco and Nayarit.

Onchocerciasis will certainly spread by the Highway if precautions are not taken, not only in the Mexican Republic, but also in the Central American States. Travel by the Highway does not involve any danger to white men, because, states the author, they apparently have a

partial immunity to onchocerciasis and must live a long time in an infected area and suffer a large number of bites of Simuliidae to be infected.

Although onchocerciasis does not endanger the life of the patient nor decrease during the first years of the disease his capacity for work, it requires the State to maintain an expensive medical service, which increases with the spread of the disease. The disease will eventually spread to such vast areas that it will be difficult to extirpate (*cf.* VAN DEN BERGHE, this *Bulletin*, who says that it cannot now be eliminated from Africa (Belgian Congo) because the bites of Simuliidae cannot be avoided and vast reservoirs of Onchocerca exist in man, buffalo and antelope). The Public Health authorities of Mexico and Guatemala began some years ago a well-planned campaign and recently established a medical investigation centre at Huixtla, Chiapas State, with a special hospital; but these efforts are local and further organizations are required.

The author advocates supervision of the movements of the population and the establishment of a well-equipped laboratory in a centre of onchocerciasis in Oaxaca or Chiapas, preferably in collaboration with scientific bodies in Guatemala and the United States; the disease may appear any day in the United States. The Simuliidae should also be studied.

A method of treating with creolin streams infested with Simuliidae is described. A barrel of this delivering 1 drop per second for 24 hours maintained a concentration of 1 in 20,000 for at least 10 km. If this were applied during the dry season in the region of the Sierra Madre of Chiapas when the number of little streams is insignificant, whole areas could be sterilized at little cost. Repetition of it twice more with an interval of 15 days would eliminate larvae born after the first treatment and also females which cannot reproduce. The method is not possible during the wet season.

The author thinks that Mexico and Guatemala can be freed of *Onchocerca volvulus*. In Chiapas State it affects some 20,000 people and in Oaxaca some 11,000. *G. Lapage.*

RAO (S. Raghavender). **Some Epidemiological Factors of Guinea-Worm Disease as Noticed in a Recent Survey of the Osmanabad District.**—*Jl. Indian Med. Assoc.* 1942. Aug. Vol. 11. No. 11. pp. 329–337. With 4 figs., 2 charts & 1 map.

A survey of guinea-worm disease in the Osmanabad district was made from the middle of April to the middle of July 1937. Villages to be surveyed were selected in such a way as to give a fair sample of the social, environmental and physical characteristics of the districts. House-to-house visits were made to record particulars of the age, sex, caste, occupation, appearance of the first symptoms, situation and number of the worms, number of attacks, movements of the patients during the two years before the attacks and the source of the drinking water. Two towns only had a modern water scheme supplying chlorinated water. The wells were examined for Cyclops. The physical features, climate and water supplies of the district are described.

The incidence of the disease for the whole population of the district is 28·9 per mille; it varied between 11·8 and 42·3 per mille; in one village it was as high as 155 per mille. Persons aged between 11 and 20 years showed the highest incidence; more than 50 per cent. of the

patients were aged 11–30 years. Out of 3,129 cases, 2,056 were males and 1,073 females. This disparity occurs in villages where the infection is endemic, but it is greater in villages where the infection is imported from other villages than in those where it is endemic. Young adults were more often attacked and children under one year were free.

One attack does not confer any immunity ; the author thinks that it renders the patient more susceptible. Nearly 67 per cent. of the 3,129 had had more than one attack ; 388 had had more than 10 attacks during 10 or more years. The highest number of attacks noted in any one individual was 50.

A table records the number of worms found ; some cases had 15 or 20 worms, but 2,086 had only one. Most worms were found in the lower extremity ; a large number were found round the ankle joints. The next most frequent site was the leg ; and the feet also were affected. When more than one worm was present, the thigh was affected. When the worm emerged at the knee ankylosis might result if sepsis occurred. The arm and the forearm were the commonest sites in the upper limb. In the trunk the worms most often appeared on the abdomen ; a few appeared on the back or chest. In a few they appeared on the external genitalia of both sexes. It is noted that the working members of a family may be disabled at a time of the year when their labour is badly needed in the fields.

Of the 434 wells examined 158 (mostly step wells) contained Cyclops. Wells were treated with 50 grains of slaked lime per gallon of water in the well, but Cyclops always reappeared in these. Experiments were done to find the best quality of lime. Surti quicklime was the best.

More than 80 per cent. of the population of this district have had the disease at one time or another. The illness usually lasts about a month but if sepsis occurs, it may last several months and deformities may result. The disease generally begins in October, reaches its maximum in March and by July new cases are hard to find, although chronic cases occur throughout the year in endemic villages.

For the prevention of the disease Rao recommends a permanent water supply for all places with a population of over 500, the substitution of draw wells for step wells, the disinfection of these wells every month between August and April, and the breeding of fish in them which will eat Cyclops (difficult because many wells dry up during the summer). *G. Lapage.*

Hosford (George N.), Stewart (M. A.) & Sugarman (Edward I.). **Eye Worm** (*Thelazia californiensis*) **Infection in Man.**—*Arch. Ophthalmology.* 1942. June. Vol. 27. No. 6. pp. 1165–1170.

This paper reports the second known case of infection of man with the Spirurid nematode *Thelazia californiensis*, a parasite which is also found in the dog and in sheep and deer. The authors think that this infection may be commoner than the records of it indicate.

The patient was a policeman, who complained of ocular fatigue and photophobia and a sensation of something moving about in his left eye. One worm was easily removed from the upper temporal quadrant of the bulbar conjunctiva. Five days later five more worms were removed from the same eye. All were females, greyish-white in colour

and 10–12 by 0·5 mm. in size, with visible transverse striations. Seven months later the eye showed no abnormality. There was no eosinophilia.

The worms are not under the conjunctiva, so that they can be easily washed out. The use of cocaine is unnecessary and may prevent the movements of the worms, so that they may be missed. They must be distinguished from *Onchocerca volvulus*, which is 2–5 times as long and is transmitted by the bites of species of Simulium ; and from *Loa loa*, which is 3–7 times as long, has no visible striations and occurs beneath the conjunctiva.

There are 20 species of Thelazia ; they lay embryonated eggs in the lachrymal duct, conjunctival sac, eye or nictitating membrane of mammals and birds. Usually they occur in both eyes in their normal hosts, but are unilateral in all cases known in man.

The only other case known of human infection with *T. californiensis* occurred in a Californian medical practitioner ; but four cases are known of human infection with the allied species, *T. callipaeda*, all of them from China. This species is found in the dog, cat, rabbit and monkey ; it causes little conjunctivitis, but markedly stimulates tear production ; intense pain and severe nervous symptoms have been reported ; the cornea may become opaque, scarification and subsequent ulceration of the cornea may be caused.

T. californiensis is known in man only in California, where infection is acquired in hilly, mountainous districts covered with brush. Infection probably occurs only during the summer. The authors think that the worms appear in the eye 3–4 weeks after infection. The life history is not known, but presumably an arthropod intermediate host is involved. *G. Lapage.*

Marble (A.), Skoog (A. P.) & Bucholz (D. J.). **Trichinosis : Report of an Outbreak at Camp Edwards, Massachusetts.**—*Milit. Surgeon.* 1942. June. Vol. 90. No. 6. pp. 636–643.

This paper is reviewed in *Bulletin of Hygiene*, 1943, Vol. 18, p. 125.

McCoy (O. R.). **The Incubation Period of Trichinosis.**—*Amer. Jl. Trop. Med.* 1942. July. Vol. 22. No. 4. pp. 313–317. With 1 fig. [12 refs.]

This paper is reviewed in *Bulletin of Hygiene*, 1943, Vol. 18, p. 128.

Spaeth (H.). Die Trichinose. Nach Beobachtungen an mehreren Gruppenerkrankungen. [**Observations on Trichiniasis in Several Groups of Patients.**]—*Deut. Med. Woch.* 1942. Sept. 11. Vol. 68. No. 37. pp. 912–916. With 2 figs. [10 refs.]

This paper is reviewed in *Bulletin of Hygiene*, 1943, Vol. 18, p. 126.

Reimann (H.). Ekg bei Trichinose. [**Electrocardiograms in Trichiniasis.**]—*Deut. Militärarzt.* 1942. July. Vol. 7. No. 7. pp. 448–454. With 6 figs.

This paper is reviewed in *Bulletin of Hygiene*, 1943, Vol. 18, p. 128.

DEFICIENCY DISEASES.

ALWALL (Nils). Ein Beitrag zu der Frage ob Ascorbinsäure im Überschuss beim Menschen Pellagra auslösen Kann. [**A Contribution to the Question whether Excess Ascorbic Acid can induce Pellagra in Man.**]—*Acta Med. Scandinavica.* 1942. Mar. 3. Vol. 110. No. 1. pp. 22–31. With 5 figs.

The present investigation was undertaken to test the statement reported by SALVESEN that vitamin C in excessive doses induces skin changes of the same type as occur in typical pellagra.

The patient was a 39-year-old woman with pronounced symptoms typical of pellagra, including psychic disturbance, anorexia, dermatitis, stomatitis, glossitis, genital and rectal affections of the mucous membrane and constipation. Six days after she arrived at the clinic she was given 0·10 gm. nicotinamide four times daily by mouth. After four days there was a distinct improvement in her condition, particularly in the mouth lesions. The nicotinamide was then reduced to two doses daily, and in addition a tablespoonful of dry yeast was given daily for three weeks. After six weeks all the symptoms of pellagra had disappeared and she was given, over a period of 62 days, an average of 1·6 gm. of ascorbic acid daily. In spite of the fact that the patient sat in the open each day exposed to the sun, and later to ultraviolet light indoors, there were no signs of the recurrence of any of the symptoms. The findings of Salvesen (who gave only 0·4 gm. ascorbic acid daily for two weeks) were thus not confirmed. *G. E. Glock.*

AHMED (N.). **Pellagra in the Upper India Provinces.**—*Jl. Indian Med. Assoc.* 1942. Oct. Vol. 12. No. 1. pp. 1–6. With 8 figs. on 2 plates.

A description of three cases and a discussion of aetiology and treatment.

SPRUE.

STANNUS (Hugh S.). **Sprue.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1942. Nov. 30. Vol. 36. No. 3. pp. 123–150. [118 refs.]

Dr. Stannus brings forward another theory as to the aetiology and pathogenesis of sprue, which is best given in his own words :—

" A. Criticisms are offered upon theories previously enunciated concerning the causation of sprue and upon some of the observations upon which they are founded.

" B. An attempt is made to suggest the lines along which a solution of the problem may lie.

" C. Evidence is adduced in favour of a theory based upon the ' partition ' hypothesis which predicates for unsplit (neutral) fat and for fatty acids a different mode of absorption from the intestine, a different route after absorption, a different composition during transport, a different destination and a different rôle in the bodily metabolism.

" D. The theory now tentatively put forward regarding the pathogeny of sprue enlists the following considerations :—

" (1) The deficient absorption of fat is limited primarily to loss of power to absorb the fatty acid moiety and cholesterol.

The author ends naïvely, Se non é vero é bene trovato [if not true, it is very ingenious]. *H. Harold Scott.*

HAEMATOLOGY.

NAYAR (Sushila). **Cholesterol and Anaemia.**—*Indian Med. Gaz.* 1942. Aug. Vol. 77. No. 8. pp. 459–469. [31 refs.]

The author confirms the findings of previous workers that the average blood cholesterol concentration of normal Indians is lower than that of Europeans, and that it is reduced in anaemias of various types and in infections.

An attempt was made to assess the therapeutic effect of intramuscular injections of cholesterol solutions in 51 cases of anaemia, mostly macrocytic anaemias of pregnancy. It was concluded that cholesterol is not effective as a substitute for liver therapy in the macrocytic anaemias, nor for iron in the microcytic types.

The author considers that there are grounds for thinking that cholesterol may exert some adjuvant action when administered together with liver or iron. *L. J. Davis.*

VAN DEN BERGHE (Louis). Contribution à la connaissance de l'hématologie normale des indigènes du Congo Belge. Premier mémoire : le sang. [**Haematology of Normal Natives of the Belgian Congo. I. The Blood.**]—*Ann. Soc. Belge de Méd. Trop.* 1941. Dec. 31. Vol. 21. No. 4. pp. 375–395. [28 refs.]

The author, working in the Belgian Congo, records the peripheral blood findings obtained in a study of 80 apparently normal natives. The subjects comprised 10 pygmies, 30 negroes living at an altitude between 1,800 and 2,000 metres, and 40 negroes, of various tribes, serving prison sentences. The latter group had been treated for intestinal parasites, but the former two groups while apparently healthy were harbouring various blood and intestinal parasites.

Haemoglobin values and red-cell counts revealed mean figures about 25 per cent. below those recorded in Europe, except in the high altitude group.

Leucocyte counts showed a general leucopenia with considerable variation in the individual counts. Differential counts revealed a relative granulocytopenia with a shift to the left and an increase in eosinophils. Price-Jones curves showed an increased mean cell diameter compared with European figures, which the author considers to be due to a racial factor.

Platelet counts were normal except among the pygmies, who displayed a thrombocytopenia.

Bleeding times, clotting times and reticulocyte counts were within normal limits. *L. J. Davis.*

CABRERA CALDERÍN (J. G.), SCULL (J. M. Labourdette) & BARRERAS (L.). **Paroxysmal Painful Crises with Abdominal Predominance in Sickle Cell Anemia.**—*Archivos Med. Infantil.* Havana. 1942. Apr., May & June. Vol. 11. p. 61. [Summary taken from *Jl. Amer. Med. Assoc.* 1942. Sept. 19. Vol. 120. No. 3. p. 243.]

Cabrera Calderín and his collaborators report the case of a Negro girl aged 11 who entered the hospital with acute abdominal symptoms.

The symptoms subsided and the girl was dismissed. One week later she had another abdominal crisis and was again sent to the hospital. Several examinations, including roentgenoscopy of the vertebral column, were negative. The blood count disclosed 2,450,000 erythrocytes, 26,000 leukocytes, 40 per cent. hemoglobin and falcular erythrocytes of sickle cell anemia. The attacks were interpreted as lumboabdominal crises of sickle cell anemia. Blood transfusion produced great improvement; the painful crises subsided, but pressure still elicited pain in the epigastric and lumbar regions. Several days later the girl had severe pain in the right elbow. This pain ceased following a blood transfusion and application of heat. Anderson and Ware ascribe the pain to splenic infarcts, stretching of the splenic capsule being the cause of pain. The articular pains are due to osseous changes. Examination of the blood is of greatest importance in the differential diagnosis, because otherwise sickle cell anemia might be mistaken for hemolytic jaundice, ovalocytic anemia, Lederer's syndrome, acute hemolysis or Cooley's anemia. Blood transfusions and liver therapy are helpful in the treatment. Possibility of sickle cell anemia should be considered in Negro patients or in half-breeds exhibiting anemia and abdominal crises.

VENOMS AND ANTIVENENES.

KELLAWAY (C. H.). **The Symptomatology and Treatment of the Bites of Australian Snakes.**—*Med. Jl. Australia.* 1942. Aug. 29. 29th Year. Vol. 2. No. 9. pp. 171–174.

This was given as a post-graduate lecture, but as the subject is not only of much interest but also one about which little is known to the general reader it demands, and merits, detailed abstract.

The dominant action of Australian snake venoms is neurotoxic, partly central, to which the nausea, vomiting, faintness and drowsiness are due, partly peripheral with paralysis of sensory and proprioceptive nerve endings and a curare-like action on motor terminals. If the phrenic end-plates are involved there comes about failure of respiration which is the commonest immediate cause of death after snake-bites in Australia. Ptosis, paralysis of the ciliary muscles and of the soft palate, and paresis of the tongue are common in the later stages.

In addition to the neurotoxic action the venoms possess a haemolytic and cytolytic property leading to the formation of lysocithin-like substances from the cell lipins and the liberation of histamine; thence arise the symptoms of circulatory failure, particularly seen after poisoning by the black snake (*Pseudechis porphyriacus*) and the copperhead (*Denisonia superba*). Some also have a coagulant action, *e.g.*, the tiger snake (*Notechis scutatus*), the brown snake (*Demansia textilis*) and the *Pseudechis porphyriacus* already mentioned. In the case of the second of these intravascular clotting may occur without direct entry of the venom into a vessel, because of its rapid diffusibility.

As with all snake poisons the symptoms vary in intensity according to amount injected, and this depends on the clothing and whether the snake has got rid of some of its poison by biting shortly before.

Weak concentrations of crude venom, therefore, stimulate the heart and affect the force of contraction; higher concentrations lead to depression and irregularity of action, and to arrest in systole. The results of neurotoxin injection differ only in that it does not lead to arrest of the heart's action. Haemolysin in large doses causes arrest, but the action here is complicated by the degree of haemolysis. Choline esterase in high concentration stimulates slightly the perfused frog's heart, but in the case of the mammalian heart injection does not affect blood-pressure, nor has it any action on respiration.

H. Harold Scott.

Pirosky (Ig.) Sampayo (R.) & Franceschi (C.). Suero anti latrodectus. I. Obtención y purificación. [**Preparation and Purification of Latrodectus Antivenene.**]—*Rev. Inst. Bacteriológ. "Dr. Carlos G. Malbran."* Buenos Aires. 1942. Sept. Vol. 11. No. 1. pp. 83–93. With 1 fig. & 1 graph. [13 refs.]

For preparing an antivenene to the poison of *Latrodectus mactans* (the Black Widow spider) the cephalothorax was separated and kept in a desiccator at 0°–5°C. Under these conditions the toxicity remained unchanged for two years. For purposes of immunization horses were used; the cephalothoraces were triturated in a mortar and mixed with physiological saline with 0·1 per cent. phenol, the final strength being one cephalothorax per cc. The first injection was 0·5 cc. Serum was obtained after 1,436 cc. had been injected in 14 weeks, and again, after the animal had had a three months' rest, when 820 cc. had been inoculated in seven weeks.

The serum was treated with 22 per cent. sodium sulphate and a precipitate obtained in which were most of the active properties; the precipitated globulins were redissolved in one-third of the original volume of saline. One cc. of the first serum was found to protect 50 per cent. of rats tested against 544 m.l.d. of the toxin, and 1 cc. of the concentrated serum against 1,200 m.l.d. The protein contents of the two sera were 6·93 and 11·33 gm. per cent. respectively.

Purification was performed by the method of peptic digestion and differential heat-coagulation (Pope's method). This product had a protein content of 7·2 per cent. and, after concentration, 6·05 per cent. One cc. of this serum would protect 50 per cent. of rats against 600 m.l.d. of the toxin and 1 cc. of the digested concentrate against 3,000 m.l.d. One gramme of the sulphate-concentrated protein would protect against 10,884 m.l.d., and of the digestion concentrate against 49,584 m.l.d. An antiserum so strong as the latter should prove of value in the treatment of human beings bitten by this spider.

H. Harold Scott.

MISCELLANEOUS.

Pessoa (Samuel B.). Ensaio sobre a distribuição geográfica de algumas endemias parasitárias no estado de São Paulo. [**Geographical Distribution of Certain Endemic Parasitic Diseases in São Paulo.**]—*Arquivos de Higiene.* Rio de Janeiro. 1941. Dec. Vol. 11. No. 2. pp. 7–25. With 9 maps. English summary.

The main interest of this article is in the series of instructive maps showing the incidence and relative intensity, by graded shading, of

ankylostomiasis, leishmaniasis, malaria and trypanosomiasis in the State of São Paulo. The prevalence of endemic disease generally is, as would be expected, greatest in those parts where rainfall and temperature are high. Hookworm infestation is only moderate [no actual figures of prevalence are given in this article, merely general statements] in the higher plains, but heavy near the shore, and, in both, attacks mostly those in the second decade of life. Five maps deal with leishmaniasis: the first two show the districts where the endemicity is high, one as it was found by Romeu DA SILVEIRA in 1914–19, the other as it was in 1941, according to the investigations of PESSOA and PESTANA; a third gives the percentage incidence in the several districts of high endemicity; a fourth demonstrates by varied shading the incidence in different parts of the State; the fifth is a map of the wooded areas showing how the zones of high endemicity and forestation on the left bank of the Tieté correspond. Alta Paulista and Alta Sorocabana to the north-west, where there are dense forests, are the areas of highest endemicity.

The author next gives a map of the Parahyba Valley and the basin of the Pinheiro and Tieté, near the capital town. This was formerly a place of "anophelism without malaria," because there anophelines were not anthropophilic; but reservoirs have been made near the town by damming up the water and these are now breeding sites for *Anopheles darlingi*. Now, only Alto de Serra and Campos de Jordao, the highlands, are free from malaria.

Chagas's disease depends not so much on climate and altitude as on housing conditions. As the woods are cleared and timber becomes scarce, the people, especially the poorer class, have to live in mud huts which harbour the vector and the disease is becoming more common. A shaded map shows the areas where infected Triatomidae have been found, where the insects are present but not infected, and those parts where there are no Triatomidae. *H. Harold Scott.*

MENDOZA (Lazaro). Paginas clinicas. [**Notes of Clinical Cases.**]—166 pp. 1942. Biblioteca Universitaria. Universidad de El Salvador, Centro America.

This publication contains a series of short papers on clinical cases seen in Salvador, Central America. Among the subjects dealt with are malaria and typhus; papers on the latter are abstracted separately in this *Bulletin*. *C. W.*

RESSELER (R.). La calcémie chez les indigènes de l'Afrique centrale. (Note préliminaire.) [**Calcaemia in Central African Natives.**]—*Ann. Soc. Belge de Méd. Trop.* 1941. Mar. 31. Vol. 21. No. 1. pp. 1–7.

DÍAZ RIVERA (R. S.), SUÁREZ (R. M.) & HERNÁNDEZ MORALES (F.). **Hypoprothrombinemia Incident to Tropical and to Non-Tropical Diseases.**—*Bol. Asoc. Med. de Puerto Rico.* 1942. May. Vol. 34. No. 5. pp. 177–182.

HSIUNG (J. C.) & KIMM (H. T.). **Tumors in Infancy and Childhood, a Statistical Study of 329 Cases in the Chinese.**—*Chinese Med. Jl.* 1942. Jan.–Feb. Vol. 61. No. 1. pp. 26–46. [42 refs.]

DAVIDSON (J.). **Flies, Fleas and Lice.**—*Med. Jl. Australia.* 1942. Aug. 15. 29th Year. Vol. 2. No. 7. pp. 111–116. [25 refs.]

HAKANSSON (E. G.). **The Use of Aqueous Smears in the Examination of Feces for Intestinal Protozoa.**—*Amer. Jl. Trop. Med.* 1942. July. Vol. 22. No. 4. pp. 325–327.

In a previous paper [this *Bulletin*, 1936, Vol. 33, p. 534] the author described the changes which the free forms of intestinal protozoa undergo when the faecal preparation containing them is made with water instead of saline. These degenerative changes are characteristic of such protozoa, so much so that they may be employed for identification purposes. In the present paper the author makes further observations on the use of the method. He notes that the presence of blastocystis frequently renders diagnosis of amoebic cysts difficult. The water method of examination, however, eliminates this, as the blastocystis quickly disintegrate, leaving the amoebic cysts more clearly visible [see this *Bulletin*, 1940, Vol. 37, p. 728]. In the water *Dientamoeba fragilis* undergoes a characteristic change. It swells for two or three minutes and then bursts, the whole of the endoplasm being discharged through the rupture in the ectoplasm. When this has occurred the ectoplasm contracts and the rupture closes, leaving the still spherical ectoplasmic shell, within which one or two granules in active Brownian movement may be seen. With further experience the author is convinced of the value of his method, which he presents as a routine laboratory procedure for the identification of the intestinal protozoa. *C. M. Wenyon.*

GHOSH (Gaurchandra). **Rural Sanitation—a Key to Success.**—*Indian Med. Gaz.* 1942. July. Vol. 77. No. 7. pp. 427–431. With 3 figs.

The author writes of the difficulty, and yet of the importance, of maintaining continuity in efforts to improve rural sanitation when these efforts depend upon voluntary cooperation of the villagers. He emphasizes the importance of sanitary inspectors, who are too often concerned only with vaccination and the collection of statistics, but who might give a lead to the people in the inauguration of simple sanitary engineering schemes. He points out that these men should be capable of drilling bored-hole latrines or tube wells, should understand drainage and the use of mosquito larvicides, should know the probable vectors of malaria in their districts, and be able to identify them, and should be able to carry out the small repairs to pumps without which so many good wells are rendered useless for long periods.

He gives samples of work which might be undertaken, and adds practical details which cannot be abstracted, but with which every sanitary inspector should be familiar :—protection of wells, chlorination of water, village drainage, soakage pits and latrines, care of cowsheds, and composting. [It is an excellent, though brief, article.]

C. W.

WAR OFFICE. ARMY MEDICAL DEPARTMENT BULLETIN. No. 15. 1942. Oct. pp. 3–5.—**Heat Stroke.**

It is noted that a healthy man, with ample supplies of water and salt, can withstand temperatures which may be dangerous to those in a state of relative dehydration and salt depletion due to gastro-intestinal derangements, or to those whose heat-regulating mechanism

has been disturbed by such infections as malaria or sandfly fever, or to men in a state of fatigue. The importance of ample water is stressed, and the suggestion is made that at centres of traffic there should be water points at which troops may obtain cold drinks and sluices. But the state of dehydration due to sweating cannot be relieved by water alone ; salt must be given, if necessary as a 0·1 per cent. solution —a not unpleasant drink.

In very hot countries there should be heat-stroke treatment centres in all camps, barracks and hospitals ; heat-stroke lorries have been useful in convoys.

A warning is given that constipation may be a result of dehydration, rather than a predisposing cause of heat stroke, and should not, therefore, heedlessly be treated by purges which cause further loss of salt and water from the bowel.

For the cooling of hospitals, wet brushwood screens have proved even more useful than fans. All febrile patients must be closely watched, since hyperpyrexia may develop suddenly. Recurrence of heat hyperpyrexia is not uncommon, and three weeks of careful treatment are necessary before a patient should be allowed to travel or to resume activity. [The question of transfer to a cooler climate should be carefully considered.] *C. W.*

BOOK REVIEWS.

Webster (Leslie T.) [M.D.]. **Rabies.**—pp. vi+168. With 8 figs. 1942. New York : The Macmillan Company. [9*s.*]

As defined in the preface the author has attempted to " fill the need for some treatise on rabies, critical, fairly inclusive but simple and available to all." He was no doubt considering chiefly an American public. As far as this country is concerned this little book should be a useful introduction to the medical or veterinary officer proceeding to a country where he may encounter the disease. It is a readable story and the essential facts about rabies are presented in a straightforward and simple fashion. The general impression conveyed by the treatment of the subject is of the " New World " with everything that is necessitarian, everything that is mechanical, striving to improve on the old tradition. In saying this it is not suggested that such an effort is not commendable. This is a far cry from the recommendation of Pliny the Elder for the treatment of the patient, that he should eat the liver of the rabid dog which bit him. Advance is still possible and Pasteur was the pioneer who paved the way.

The author expounds at some length on vaccines and cauterization in the prevention of rabies following exposure to infection. He states that " in the absence of treatment the chances of an exposed person's contracting rabies are unknown " and that " critical experimental evidence of the efficacy of vaccine treatment is lacking." A member of the " general public " reading the book might therefore think he could well revert to " Les remèdes charitables de Madame Fouquet." Expecially in these stringent times, he might even consider it worth while to be bitten by a rabid dog if the remedies were a royal dish consisting of an " omelette aux écailles d'huitres pilées avec la poudre de pimprenelle " to be washed down with a bottle of Chablis and a

journey to the " plages " of the Mediterranean or Dieppe to indulge in frequent bathing " avant que le venin ait pénétré jusqu'aux parties nobles." However, in this present book, if he reads on, he notes that " against this, however, are McKendrick's statistics that if a person is bitten by a rabid dog and takes treatment his chances of contracting rabies are no more than 1 in 77 and usually as low as 1 in 510 " and therefore " persons exposed to rabies should be given vaccine treatment with confidence that then there is small likelihood of development of the disease." This should overcome any misgivings that may have arisen in his mind from the information given to him perhaps unwisely on pages 95 and 96 that " untoward effects of rabies treatment are too numerous to be ignored and that post-vaccinal paralysis may appear which may be transient, prolonged or fatal." The mind of the enquiring member of the general public is not likely to be cleared even when he is brought up with a jerk by the statement, " Right here it should be made plain that McKendrick's carefully compiled and analysed statistics were designed to compare the effectiveness of anti-rabies vaccines and not to answer the question whether vaccine does or does not protect against rabies. Indeed it is problematical whether mortality rates among treated persons can throw light on the effect of treatment."

Errors of any sort are few. Surely it is the printer and not the author who is responsible for the statement (page 17) that the virus remains active " for at least 30 days in glycerine at 40°C. [? 4°C.]," and the author would not suggest (page 95) that the " low morality " may be due either to the treatment itself or to the resistance of the individual exposed.

Within the small compass of 167 pages there are chapters on (1) Rabies in animals and man, (2) Is rabies a myth ? (3) The cause of rabies, (4) How the virus causes rabies, (5) How the virus damages the host, (6) The diagnosis of rabies, (7) History and epidemiology of rabies, (8) Prevention of rabies prior to exposure, (9) Evaluation of rabies vaccines, and (10) Prevention of rabies following exposure.

The necessity of the control of the dog is emphasized by the inclusion of appendices on the licensing, confinement and disposal of vicious and rabid dogs. The more rare but not less important parts played by the mongoose in South Africa and the vampire bats in South America, in transmitting rabies, have not been forgotten. The comparatively recent realization of the usefulness of the white mouse for the diagnosis of rabies and the estimation of the potency of rabies vaccines has also been stressed. Cauterization with nitric acid of the wound caused by a bite is an " established routine " which according to this book appears to have survived in the " new " world.

It would appear that the author has tried to provide for too wide a public (*v.* preface page vi :—" dog owner and general public but also veterinarian, physician and student of virus diseases "). The student of virus diseases or laboratory worker would, for example, look in vain for a full and concise description of technical methods employed in the diagnosis of rabies. He would probably wish to know more of the properties of the virus, but he might be consoled with appendix vi which deals with " a subject of theoretical rather than practical interest " *viz.* " Rabies antibodies and their relation to immunity." If not he must use the book as a key to the scientific literature in the 62 references of the bibliography, and to the text-books referred to in a footnote on page 32.

The public health officer may feel that if the dog owner and general public read it, he will not have to answer so many questions or cover the same ground so often. The physician, however, at least on this side of the Atlantic, would no doubt look on so much popular science and outspoken frankness to the layman as inadvisable. During a course of vaccine injections following the bite of a rabid animal the favourable psychological state of the patient is an all-important factor contributing to a successful issue. The physician would no doubt prefer that his patient knew less about prognosis and possible sequelae.

There is much in the book which is useful, yet some of us may feel that a book about rabies which omits reference to Meister, "le petit berger Jupille" and "la vieille écurie de Villeneuve l'Étang" while it may be practical and up to date, lacks something which the modern bacteriological research worker at least should not be allowed to forget, "l'ésprit Pastorien," to which he owes so much. *I. A. Galloway.*

Belding (David L.) [M.D., Professor of Bacteriology and Experimental Pathology, Boston Univ. School of Med., etc.]. **Textbook of Clinical Parasitology, including Laboratory Identification and Technic.**—pp. xxi+888. With 279 figs. and 4 coloured plates. 1942. New York and London: D. Appleton-Century Company, Inc. [45*s.*]

The author of this treatise has drawn freely but with method on the best available sources, chiefly in the American and British literature. As he himself puts it "The writer has approached the subject not as a specialist, but from the broad viewpoint of a biologist with a medical background, who has followed for many years the teaching of parasitology to medical students."

His book gives a well arranged and straightforward account of medical parasitology in a very wide sense, both the parasites and their vectors being dealt with in an adequate manner. The diagrams are numerous and clear, the coloured plates and photographs excellent, and the tables most helpful. To each section is appended a list of the more important references. The volume ends with a chapter on technical methods and treatment. Recent work is included, for example, Rao and Maplestone's description of the male and female adults of *Wuchereria malayi*.

Bearing in mind certain limitations which the author himself indicates, it may be said that parasitologists will find here information on almost all matters with which they are likely to have to deal. Neither rat-bite fever nor *Spirillum minus* appears in the index nor has the reviewer been able to trace them in the text. The same remarks apply to *Leptospira icterohaemorrhagiae* and spirochaetal jaundice. Although these cosmopolitan diseases of man are omitted, there is more than a passing reference to certain diseases and parasites of animals, *e.g.*, Texas fever, *Babesia bigemina* and *Spironema gallinarum*. Yaws receives rather scant mention considering its great prevalence and the serious nature of its effects.

Blanfordia is retained, *e.g.*, *B. formosana* and *B. nosophora*, as the name of snails concerned with the transmission of *Schistosoma japonicum*. *Borrelia* is adopted as the generic term instead of *Spirochaeta* for the relapsing fever parasites, *e.g.*, *B. recurrentis* and *B. duttoni*; *Treponema pertenue* is used for the parasite of yaws.

The ever-changing nomenclature of parasites and their transmitting agents will find any author at fault on some occasions. It may be said that in this volume these occasions are few in number for such a compendious work. *Mansonia annulatus*, *Anopheles albopictus* and several other obvious slips of similar nature are to be found. The use of the specific name *Anopheles costalis* may be regarded either as anachronistic or as an example of legitimate prophecy—one never knows what the creature's name may prove to be eventually. In any case the printer's modification of it—*Anopheles coastalis* (p. 656)—is first class, and can hardly fail in its nostalgic appeal to those who are familiar with West Africa.

This volume is certain to prove of great service to medical men engaged in work in the tropics and subtropics. Many laboratories will doubtless soon be set up in the East ; there the book will be found particularly useful because of the good account it gives of the parasites which may be found in China and other Far Eastern countries.

D. B. Blacklock.

ALVARADO (Carlos Alberto). **Tratamiento del paludismo.** [Treatment of Malaria.]—90 pp. With 2 folding coloured figs. [Bibliography.] 1941. Buenos Aires : Libreria y Editorial " El Ateneo," Florida 344–Cordoba 2099.

The author, who is the Director General of Malaria in the National Health Department of the Argentine, has written a condensed account of malaria and its treatment. With the aid of two excellent coloured plates the characteristics of the three forms of malaria parasite are described, and the asexual and sexual cycles of development of the parasite are outlined. The main part of the small book is concerned with the therapeutics of malaria. Treatment, both general and symptomatic, is adequately dealt with. There are also chapters on collective treatment and drug prophylaxis of malaria. There is small room for originality in the preparation of a book of this kind, but the author has selected his facts with care, and his teaching is clear and concise.

Norman White.

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